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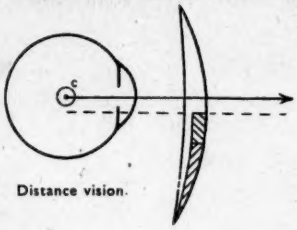
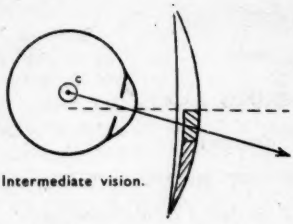
FUSED TRIFOCAL LENSES

Presbyopes with a reading addition of +1.50D or more, often experience difficulty in becoming accustomed to the sudden change of power between the two portions of bifocal lenses.

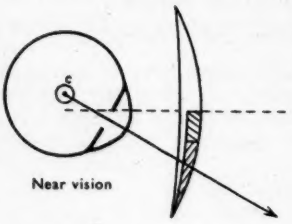
Trifocal lenses, which are made in fused form, present an intermediate portion whose power is exactly half-way between those of the distance and reading portions. This intermediate portion, as well as lessening the call on accommodation, markedly diminishes the "jump" experienced with the usual type of bifocal lens, due to lack of correspondence of the two centres; in this respect trifocal lenses are comparable with Hamblin's "No-jump" bifocals. The elimination by trifocal lenses of that intermediate zone in which an advanced presbyope is otherwise unable to focus his vision has led to their becoming known in America as "continuous vision lenses".



Distance vision.



Intermediate vision.



Near vision

c = centre of rotation

Trifocals, often desirable, become invaluable to presbyopes in those occupations necessitating clear vision of that part of the foreground which is outside their reading distance. Wearers such as painters, who work largely at arm's length and those who must interview other people, as must most professional men, find these lenses of particular service.

The diagrams show the principles of fitting trifocals, a procedure requiring considerable care. Hamblin's, in over twenty years' experience of dispensing them, have been impressed by the readiness with which presbyopes, although unsatisfied by bifocals, will accept trifocal lenses.

In order to enable more surgeons and patients to become familiar with their advantages, Hamblin's will willingly replace with bifocals any trifocals fitted by them and not found satisfactory. No charge will be made for this service, but the patient should have worn the glasses for a trial period of six weeks and should return them in good condition within a further two weeks if he wishes to have them replaced.

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Brit. J. Ophthal. (1953) 37, 129.

COMMUNICATIONS

CENTRAL AREOLAR CHOROIDAL SCLEROSIS*

BY

ARNOLD SORSBY AND R. P. CRICK

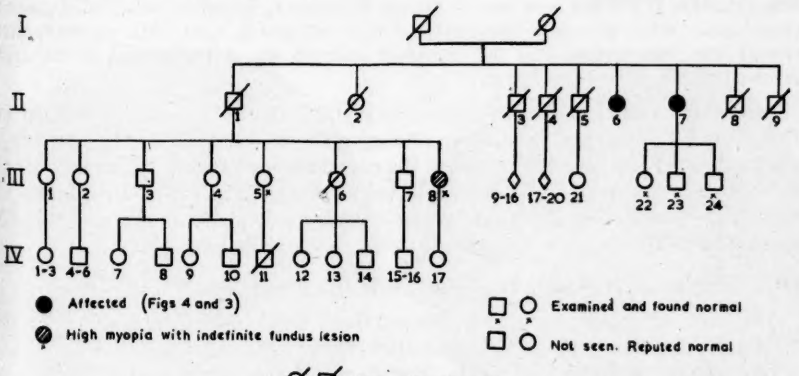
London

IN an earlier study (Sorsby, 1939) attention was drawn to the genetic nature of central choroidal sclerosis, a condition known in the literature as central senile areolar choroidal atrophy. An account was given of the occurrence of this condition in two brothers, aged 59 and 63 years respectively (Figs 1 and 2, p. 135). Both patients gave a history of visual disturbance beginning at about the age of 20, and worsening progressively. As no other members of the family were affected, there was no opportunity of studying the appearances of the disorder in the earlier or later stages, nor could anything definite be said as to the mode of inheritance. Four further families are now reported, considerably extending the range of ophthalmoscopic appearances—supported in one case by histological material—but leaving the mode of inheritance still undecided.

Case Reports

(1) B . . . n Sibship (Pedigree Chart I; Figs 3 and 4).

Two sisters, the sole survivors of a sibship of nine (whose parents were not related) were seen and found to be affected.



PEDIGREE CHART I.—B . . . n sibship.

* Received for publication November 7, 1952.

FIG. 3.—Left fundus of Mrs. Sarah Cl., aged 70 (B II, 7).

FIG. 4.—Left fundus of Miss Elizabeth B., aged 72 (B II, 6), sister of B II, 7 (Fig. 3).

(*i*) *Mrs. Sarah Cl.* (B II, 7), was first seen in February, 1946, at the age of 70 (Fig. 3). Visual acuity: 1/60 in the right eye, hand movements in the left.

Her vision had been poor since about the age of 20, and had deteriorated steadily, especially in the last 3 or 4 years. Refraction: emmetropic. The fundi show exposure of the choroidal vessels over the central area, with some evidence of sclerosis (Fig. 3). When the patient was seen again in April, 1948, there was no substantial change.

(*ii*) *Miss Elizabeth B.* (B II, 6), sister of the above and 2 years older, showed the same type of central lesion (Fig. 4).

Visual acuity: 1/60 in each eye. Refraction: right +2.0 D. cyl. at 120°, left +1.0 D. sph. ⊃ +1.50 D. cyl. at 60°.

The fundus lesion was rather smaller than in B II, 7, but evidence of sclerosis was more marked. Here, too, there was a history of failing vision from about the age of 20. When she was 35 she had been seen by the late Reginald E. Bickerton, who found central choroiditis. When she was re-examined in April, 1948, and in April, 1951, no substantial change was seen, except that the choroidal sclerosis was more marked in the area involved, which itself was no larger.

In neither case was there any history of nightblindness. The three children of B II, 7—a daughter aged 48 and two sons aged 45 and 44 (B III, 12, 13, and 14)—were examined and found normal, but the collateral branches of the family proved difficult to follow up. A reputedly affected niece aged 39 (B III, 8) was found to be a high myope with extensive fundus changes difficult to interpret. Her six living sibs (B III, 1–5, and 7), aged 41 to 62, were reputed normal.

(2) C . . . n-C . . . . l Sibship (Pedigree Chart II; Figs 5–9).

The affected sibship originally consisted of seven members, one of whom (C III, 6) died when young. The parents were not consanguineous. The mother is recorded to have had bad sight. The six survivors were seen and five found to be affected (C III, 1, 2, 3, 4, and 5). None of the affected members who were aged 58, 56, 54, 52, and 50 respectively complained of nightblindness. The eldest (C III, 1) was unconscious of eye trouble; C III, 2 had been registered as

FIG. 5.

FIG. 7.

FIG. 8.

FIG. 9.

FIG. 13.

FIG. 14.

FIG. 5.—Right fundus of Mrs Bertha C., aged 56 (C III, 2).

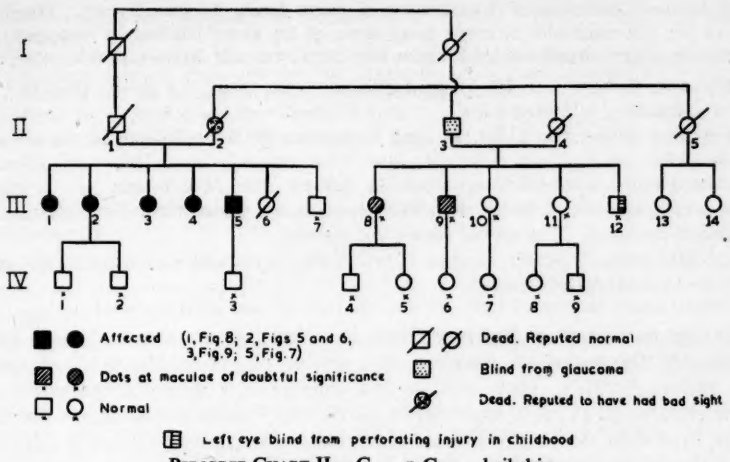
FIG. 8.—Right fundus of Miss Esther Co., aged 60 (C III, 1), sister of C III, 2 and 5 (Figs 7 and 5).

FIG. 13.—Left fundus of Mrs. Charlotte Bu., aged 58 (Br II, 3).

FIG. 7.—Right fundus of Robert Co., aged 50 (C III, 5), proband, brother of C III, 2 (Fig. 5).

FIG. 9.—Left fundus of Miss Helena Co., aged 54 (C III, 3), sister of C III, 1, 2, and 5 (Figs 8, 7, and 5).

FIG. 14.—Left fundus of Mrs. Gladys Br., aged 30 (Br III, 3), proband, daughter of Br II, 3. (Fig. 13).


I
II
III
IV
Affected (I, Fig. 8; 2, Figs. 5 and 6; 3, Fig. 9; 5, Fig. 7)
Dots at maculae of doubtful significance
Normal
Dead. Reputed normal
Blind from glaucoma
Dead. Reputed to have had bad sight
Left eye blind from perforating injury in childhood

PEDIGREE CHART II.—C . . . n-C . . . . l sibship.

blind for some 2½ years, her sight having begun to fail some few years before; C III, 3 suspected that she might have some trouble; C III, 4 had had eye trouble for some indefinite time; C III, 5 (the proband) had almost full vision in each eye.

Two of the five, therefore, showed the fully developed picture, but vision was severely affected in only one, and three who were in the earlier stages of the affection showed only mild visual disturbances. It should be noted that there is no direct chronological sequence. The appearances in this sibship in order of severity were as follows:

(*i*) *Mrs. Bertha C.* (C III, 2) aged 56, certified blind (Figs 5 and 6).

Visual acuity: counting fingers in each eye; myopia of about 8 D.

She first noticed poor sight at the age of 12 (but this probably represents the onset of her myopia), and became conscious of serious deterioration of vision at about the age of 52. The fundi show myopic crescents and a typical central areolar choroidal sclerosis surrounded by fine pigmentary mottling.

FIG. 6.—Left fundus of Mrs. Bertha C. (C III, 2). Her right fundus is shown in colour (Fig. 5). Both fundi in this patient are shown because the two eyes are the subject of a pathological report (Ashton, 1953, p. 140 of this issue of the *B.J.O.*)

She died suddenly in December, 1951, from coronary thrombosis, and the *post-mortem* findings are the subject of a separate communication in this issue (Ashton, 1953, p. 140). Her two sons (C IV, 1 and 2) aged 26 and 21, are normal.

(*ii*) *Robert Co.* (C III, 5), aged 50, proband (Fig. 7).

Visual acuity (with correction); 6/9 in the right eye and 6/6 pt. in the left. Refraction: −1.50 D. each eye.

He has been conscious of deterioration of vision during the past 8 years. His fundus lesions are not markedly different from those of his sister. When he was seen again 18 months later in April, 1951, his vision with correction had declined to 6/36 in each eye.

(*iii*) *Miss Esther Co.* (C III, 1), aged 60 is not aware of any eye trouble (Fig. 8).

Visual acuity: 6/12 in each eye.

(*iv*) *Miss Helena Co.* (C III, 3), aged 54 has recently noticed some failure of the left eye (Fig. 9).

Visual acuity (with correction): 6/9 in the right eye and 6/24 in the left.

Both central areas, of the left more than the right, are somewhat oedematous and show exudative reactions. The retinal vessels are normal.

(*v*) *Miss Kitty Co.* (C III, 4), aged 52 lives in New York and is reported by Dr. Milton Berliner to show central lesions.

Visual acuity (with correction): 20/70 in the right eye and 20/50 in the left.

As can be seen from Pedigree Chart II, a brother and sister, children of first cousins (C III, 8 and 9)—members of a sibship of five (C III, 8–12) all seen by Dr. Milton Berliner—show mild central changes of a doubtful character; their three children (C IV, 4, 5, and 6) aged 22, 19, and 7 years, are normal. The father (C II, 3) of these doubtfully affected individuals, who is himself a cousin of (C II, 1) the father of the collateral branch, is blind from glaucoma and has no fundus lesion.

(3) H . . . s Sibship (Pedigree Chart III; Figs 10–12).

The parents were first cousins and there was an indefinite history of eye trouble in the father's mother. The sibship consisted of six members. H II, 4 died at the age of 48 from carcinoma of the gall bladder, having entered a blind home at the age of 32 on account of trouble reputed to date from about the age of 15. H II, 5 died from tuberculosis at the age of 30 with no history of eye trouble. The proband (H II, 2) was aged 65, and in her case the diagnosis of central areolar choroidal sclerosis was not made until her younger brother (H II, 3) was found to show a typical lesion. The four survivors are apparently all affected:

(*i*) *Arthur H.* (H II, 3), aged 63 noticed difficulty in reading at the age of 36, and this has become progressively worse. He has no nightblindness (Fig. 10).

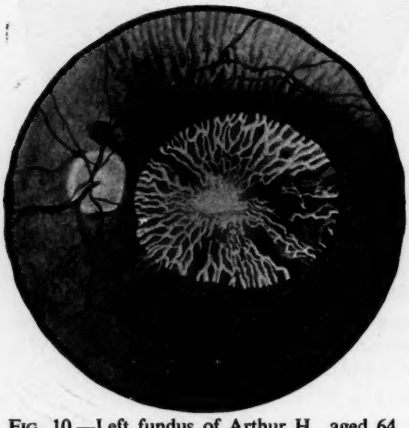
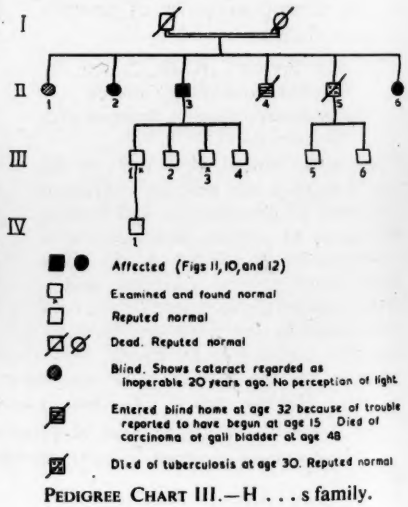


FIG. 10.—Left fundus of Arthur H., aged 64 (H II, 3).



PEDIGREE CHART III.—H . . . s family.

Visual acuity: hand movements in the right eye at 1′ with c̄ −2.5 sph. ⊃ −1.0 cyl. at 110°; in the left eye it is 6/60 with c̄ 1.75 sph. ⊃ −2.0 cyl. at 100°.

Fields: right not practicable, left to 10/1,000 white shows peripheral constriction marked on the temporal side and joining up with the blind spot, and a central scotoma.

Colour vision: no perception of any colour on Ishihara test.

General health good except for "gastric trouble".

In the left fundus (Fig. 10), the discs are pale with shallow cupping and atrophic crescents, the retinal vessels are attenuated, and an areolar patch of choroidal sclerosis is seen in the central area with sharply defined edges. There is some generalized choroidal sclerosis peripherally with a few streaks of pigment, some in the shape of bone corpuscles.

Two of this patient's four sons (H III, 1 and 3) aged 34 and 30 were found to be normal; the two other sons (H III, 2 and 4) aged 31 and 27 could not be seen but were reputed normal.

(ii) Miss Edith H. (H II, 2) aged 65, proband, had had poor vision for many years. She had recently noticed a black spot floating in front of the left eye, but did not complain of nightblindness.

Visual acuity: 3/60 in the right eye with c̄ +3.5 sph. ⊃ +2.0 cyl. at 125° = 6/60; in the left eye it is 2/60, with c̄ +3.5 sph. ⊃ + 1.75 cyl. at 70° = 6/60.

Fields: full to confrontation.

Dark adaptation (Crookes adaptometer): normal curve.

Colour vision: no perception of any colour on Ishihara test.

Pigmentary changes in the central area of both fundi were seen against a circular background of whitish-grey dots. This was initially diagnosed as a macular dystrophy. *Some white dots were also present at the periphery. The choroidal vessels were not* exposed (Fig. 11).

(iii) Mrs. Nellie K. (H II, 6) aged 55, reported failure of vision from about the age of 37, but no nightblindness.

Visual acuity: 6/60 in the right eye with c +3.5 sph. ⊃ + 1.0 cyl. at 180°; in the left eye it was 6/60 with c̄ +3.5 sph. ⊃ +2.5 cyl. at 180°.

Fields: right and left central scotomata.

Colour vision: no perception of any colour on Ishihara test (Plate 1 only was recognized).

Both fundi show central changes consisting of slight general pallor associated with very fine pigmentary stippling (Fig. 12). *This patient has no children.*

FIG. 11.—Right fundus of Miss Edith H., aged 66 (H II, 2), proband, sister of H II, 3 (Fig. 10).

FIG. 12.—Left fundus of Mrs. Nellie K. (H II, 6), sister of H II, 3 (Fig. 10) and H II, 2 (Fig. 11). Her right eye showed definite outlying choroidal sclerosis near the central area.

(*iv*) *Miss Emily H.* (H II, 1) aged 71, the eldest sister, is totally blind; her sight began to fail at about the age of 30 and she was blind by the age of 40. She does not remember nightblindness as a feature in her developing troubles. Both eyes show mature cataract, dilated pupils, normal tension, and no perception of light.

(4) B....t Family (Pedigree Chart IV; Figs 13 and 14).

Of the three sibs, two are non-identical twins (one twin being the proband). The other two sibs are normal, but the mother is affected. The mother and father are not consanguineous.

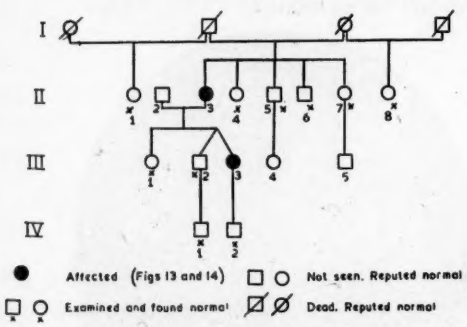
(*i*) *Mrs. Charlotte Bu.* (*née* C . . . k), (Br II, 3) aged 58, mother of proband (Br III, 3).
Visual acuity in each eye is 5/60. Refraction: right +0.75 D., left +1.0 D. Not improved.
Colour vision: no response to Ishihara test.
Ilford anomaloscope reading: 38/25–80.

Her sight failed in the early forties, and appears to have remained stationary since. The left fundus (Fig. 13) shows a sharply circumscribed oval patch of central choroidal sclerosis but not the typical end-stage of conversion into white streaks. There is fine pigmentary mottling around the circular patch.

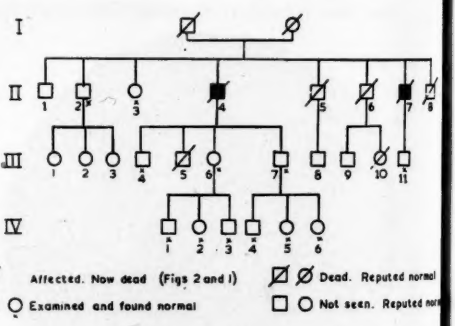
(*ii*) *Mrs. Gladys Br.* (Br III, 3) aged 30, proband, presented herself because of failure in sight over the past year and was regarded as a case of possibly dominant macular dystrophy.
Visual acuity: 6/36 in each eye. Refraction: right +1.50 D., left +3.0 D. Not improved.
Colour vision: Ishihara test normal.
Anomaloscope reading 38/60.

The left fundus (Fig. 14) shows a number of discreet white dots scattered over the periphery, and some fine pigmentary mottling around the central area, which itself has a washed-out appearance, suggestive of an earlier stage of the lesion seen in Br II, 3.

No other affected person was found amongst the mother's four sibs (Br II, 4–7), nor were her two half-sisters affected—one being on the mother's side (Br II, 1), and the other on the father's side (Br II, 8). The proband's brother and sister (Br III, 1 and 2) were also found to be normal.



PEDIGREE CHART IV.—B....t family.



PEDIGREE CHART V.—R . . h family.

(5) Follow-up of R . . h Sibship originally recorded in 1939 (Pedigree Chart V; Figs 1 and 2).

The two affected brothers (R II, 4, and 7; Figs 1 and 2) are now dead. No other surviving member of the sibship is affected. The three surviving descendants of the elder affected brother, (R III, 4, 6, and 7) aged 55, 47, and

43 years, were found to be unaffected. The only son of the younger affected brother, (R III, 11) who could not be traced, had been normal when seen in 1938 at the age of 22 years.

FIG. 1.—Left fundus of George R., aged 59 (R II, 7). *See B.J.O.* (1939), **23**, 433, Fig. 2. In this patient, as in all except H II, 6 (Fig. 12), the appearances were almost identical in each eye.

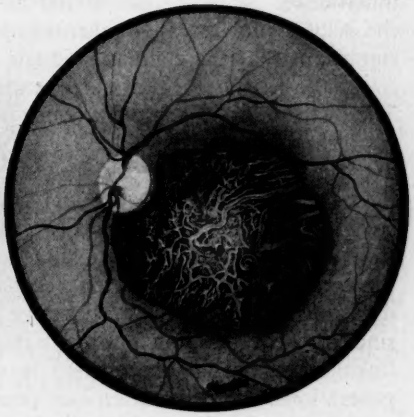


FIG. 2.—Left fundus of Richard R., aged 63 (R II, 4), brother of R II, 7 (Fig. 1). *See B.J.O.* (1939), **23**, 433, Fig. 4.

Discussion

(1) Mode of Inheritance.—In the five families available the outstanding genetic facts are these:

(1) The affection has been observed in only one generation in four of the families, and over two generations in one family.

(2) Consanguinity has been noted in only one family, the parents being first cousins.

There is some indefinite evidence of the affection in collateral branches in two families. In the C . . n-C . . . . 1 sibship (Pedigree Chart II) it is possible that two cousins of the affected sibship are also affected, these collateral branches being descended from two sisters (C II, 2 and 4) who married men who were themselves first cousins (C II, 1 and 3), though unrelated to the sisters' family. Furthermore, there is some suggestion of transmission over two generations: C II, 2, the deceased mother of one of the sibships, is reputed to have had bad sight, the nature of which could not be determined; the father of the second sibship (C II, 3) likewise has eye trouble, and has been found to be suffering from glaucoma.

Some suggestion of the affection in a collateral branch is also seen in the B . . . n sibship (Pedigree Chart I); B III, 8, a niece of the affected women (B II, 6 and 7), has high myopia with indefinite fundus lesions.

The four families in which the affection has been observed in one generation only present no conclusive evidence regarding the mode of inheritance. The consanguinity in one family is at best suggestive only of recessive inheritance. If the collateral branch in Pedigree Chart II is indeed affected, the evidence for recessive inheritance becomes more convincing. It may be significant that the eight individuals aged more than 30 (six of them were over 40), all offspring of three known affected persons, were all normal. The distribution of the disturbance in the affected generations of these four families (as analysed in the Table) shows, however, a considerable excess over the 25 per cent. affected theoretically expected with recessive inheritance, there being sixteen affected and seventeen unaffected. If the analysis is confined to individuals actually examined, the excess and the departure from expectation becomes still more marked—twelve affected and six unaffected. Whilst autosomal recessive inheritance is possible, the available data do not fit too well. Recessive sex-linkage can obviously be excluded, since the twelve known affected include eight women. Intermediate sex-linkage can hardly be assessed in the absence of observations over two generations. Sex-limitation—or possible intermediate sex-linkage with the carrier state manifested by pathological but milder lesions—is not excluded, for there were in all fifteen individuals in affected sibships on whom full information was available: six men, of whom four were affected, and nine women, of whom eight were affected. The four affected men—by no means the oldest in the series—all showed a severe lesion, to which only one of those in the eight affected women was at all comparable. The theoretical possibilities that the pathogenic gene is carried either on disjointed XX chromosomes, or on the Y chromosome of such women, are excluded by the sex distribution in the affected sibships.

TABLE

DISTRIBUTION IN THE AFFECTED SIBSHIPS

Sibship	Affected		Possibly affected		Unaffected		Unknown, but probably unaffected		No information	
	M	F	M	F	M	F	M	F	M	F
B . . . n	—	2	—	—	—	—	6	1	—	—
C . . n-C . . . l (*a*)	1	4	—	—	1	—	—	—	—	—
(*b*)	—	—	1	1	1	2	—	—	—	—
H . . . s	1	2	1	1	—	—	1	—	—	—
R . . h	2	—	—	—	1	1	3	—	1	—
Total ...	4	8	2	2	3	3	10	1	1	—

The one family showing an affected mother and daughter—the mother and her husband not being consanguineous—raises the possibility of dominant

inheritance—a possibility that is neither proved nor disproved by the appearance of only one case amongst the three children. The fact that the mother's two half-sisters—one on the father's side and one on the mother's side—are unaffected gives no support for dominant inheritance, but does not exclude it. Nor is dominance excluded by the fact that this mother's four full sibs are also unaffected.

(2) Age of Onset.—It would seem that ophthalmoscopically visible lesions may be present for some years without serious symptoms. This is borne out in the C . . . n-C . . . l family, where C III, 1, 3, and 4, all aged over 50, show lesions without marked subjective symptoms. On the other hand, in the B . . . n sibship and in the R . . h sibships, definite and progressive trouble dated back to the early twenties. The C . . . n-C . . . l sibship and the H . . . . s sibship both show that within the same family severity of lesion and symptoms is not determined by age. It is therefore difficult to indicate a definite age of onset: a range of ages between 20 and 50 years for the onset of symptoms has been observed, and in contrast objective lesions without serious visual trouble have been noted in patients in the fifties.

(3) Ophthalmoscopic Changes.—The most severe changes are those observed in the R . . h sibship previously recorded. In the B . . . n sibship (Chart I) the changes are distinctly less marked. In the C . . . n-C . . . l sibship (Chart II) severe ophthalmoscopic lesions are evident in two patients, but consist of little more than mild central exudative reactions in three others. Likewise in the H . . . s sibship (Chart III) and in the B . . . . t family (Chart IV) both the full picture and early changes are seen. Taking these five groups together the following considerations emerge:

(*i*) *Course.*—It would appear that the earliest changes are oedematous-exudative reactions in the macular and paramacular areas (Figs 8 and 9), or an atrophic reaction at the macula with mottling and exudative reactions around it (Figs 11, 12, and 14). These stages show nothing pathognomonic, and might well be mistaken for a macular dystrophy or a central chorio-retinal lesion of environmental origin. Exposure of the choroidal vessels and their conversion into white streaks represent a later stage (Figs 3, 4, and 13) when a definite diagnosis becomes possible. The most marked stage in this series is the showing up of the chorio-capillaries as a white network, with some extension of the choroidal sclerosis beyond the sharply delineated central lesion (Figs 1, 2, 5, 6, 7, and 10).

(*ii*) *Changes in Relation to Age.*—In two families (R . . h and B . . . n sibships) only the fully developed picture was observed, more marked in the R . . h brothers (R II, 7 and 4; Figs 1 and 2), who were aged around 60 years, than in the B . . . n sisters (B II, 7 and 6; Figs 3 and 4) who were some 10–15 years older.

In the C . . . n-C. . . . l sibship the fully developed picture was present in two individuals, a sister (C III, 2) aged 56, and a brother (C III, 5) aged 50 (Figs 5, 6, and 7), whilst a non-specific oedematous-exudative reaction was present in three other aged 58, 54, and 52 years (C III, 1, 3, and 4; Figs 8 and 9). Likewise in the H . . . . s sibship the patient who showed the full

lesion (H II, 3; Fig. 10) was aged 63 years, whilst one of his sisters, 2 years older, showed a distinctly earlier and uncharacteristic stage (H II, 2; Fig. 11). That the affection is progressive is shown by the appearances in the mother and daughter in the B....t family (Br II, 3 and Br III, 3; Figs 13 and 14), but a strict chronological order is not a feature of the disturbance.

(4) Pathology.—Clinically the lesions suggest occlusion of the choroidal vessels in the central area, and the designation of central choroidal sclerosis seems justified, but the histological study of the eyes of C III, 2, does not appear to bear this out. There was evidence of atrophy of the vessels rather than of angiosclerosis; this is fully discussed in the accompanying study by Ashton (1953).

(5) Clinical Features and Course of the Affection.—No final assessment is as yet possible. For the present the following appears to be valid:

(*i*) *Mode of Inheritance.*—This yet remains to be established.

(*ii*) *Age of Onset.*—In two families this appears to have been at about 20. In one family there is evidence that subjective symptoms may not develop until about the age of 50, though ophthalmoscopic lesions were already present.

(*iii*) *Ophthalmoscopic Course.*—The earliest changes appear to be of the nature of a "central choroiditis". The lesion begins as a mottling or an oedematous-exudative reaction of the whole of the central area. This appears to progress only slowly towards exposure of the choroidal vessels and their conversion into white streaks. Severity is not strictly related to age.

(*iv*) *Subjective Symptoms.*—Central vision deteriorates to 6/60 or less. The peripheral fields remain intact and there is no nightblindness. Colour anomalies appear to set in only when vision is grossly reduced.

(*v*) *Designation.*—The classical designation "central senile areolar choroidal atrophy" is unwarranted in so far as it stresses senility and atrophy as essential features. It is only in old age that the advanced stage of central areolar choroidal sclerosis has been recognized, but the affection itself is essentially one of early and middle life, with central exudative or mottling reactions rather than atrophy. "Central areolar choroidal sclerosis" would appear to be a more satisfactory designation, even if at the present there is no supporting histological evidence to incriminate sclerosis of the choroidal vessels.

(*vi*) *Differential Diagnosis.*—The fully developed picture of central areolar choroidal sclerosis is unmistakable, because its three components are clearly defined: the central position, the characteristic changes in the exposed choroidal vessels, and the sharp demarcation of the lesion from the surrounding background.

No difficulty arises in differentiating the lesion from generalized choroidal sclerosis, nor from isolated extra-central patches. Where, however, there is a patch of choroidal sclerosis confined more or less to the central area, difficulty in diagnosis arises. Patches of central choroidal sclerosis are not uncommon in generalized fundus dystrophy, but the families with this latter affection so far reported (Sorsby and Mason, 1949, and Burn, 1950), though they show choroidal sclerosis in the central area, all lack the sharp limitation and areolar stamp seen in the present series. Moreover, the dominant course and the definite age of

onset of generalized fundus dystrophy are useful distinguishing features. No difficulty is likely to arise with choroidal sclerosis consequent on an old inflammatory reaction, or on injury. These are not usually bilateral and central, seldom—if ever— areolar in type, and occasionally are multiple or sectorial.

In contrast, the early stages of the affection show little that is pathognomonic. Their genetic character may be suspected by the symmetry and similarity of the lesion in the two eyes. The mottling reaction can readily be mistaken for macular dystrophy or the earlier stages of generalized fundus dystrophy, whilst the oedematous-exudative reaction is not unlike that seen typically in the latter affection.

Summary

(1) Four further families showing central areolar choroidal sclerosis are reported, and a follow-up of the sibship originally recorded in 1939 is given.

(2) In four of these families the affection was observed in sibships only. In one family it was seen in a mother and daughter.

(3) The fourteen observed cases show several stages of the affection. The earliest ophthalmoscopic appearances are an exudative-oedematous reaction centrally, simulating the early stages of generalized fundus dystrophy, or a pigmentary mottling of the central area simulating macular dystrophy. The lesion becomes pathognomonic when there is exposure of the choroidal vessels centrally over an areolar area. This progresses to ophthalmoscopically visible obliteration of these exposed choroidal vessels and choriocapillaries. The age of onset seems to vary in different families. In two families it began in the early twenties; in one in the late forties. In a fourth family nothing definite could be determined. The fully established lesion has not been seen in any patient under the age of 50. The lesion appeared to be more severe in all the four affected men than in all but one of the ten affected women, though the affected men were not the oldest in this series.

(4) The available evidence is conclusive as to the genetic character of the affection, but not sufficiently extensive to establish the mode of inheritance.

Dr. J. S. Cotman of East Peckham, Kent, and Mr. T. H. Tizzard of Bath kindly helped with information on the R . . h family. Mr. D. H. Teasdale of St. James's Hospital and the Blind Welfare Department of the London County Council supplied records on a member of the H . . . . s family, and Mr. W. S. Burr of Plymouth a report on a member of the B . . . . t family. Mr. J. B. Davey and Dr. Ruby Joseph helped in following up some of the families.

We are particularly indebted to Dr. Milton Berliner of New York for kindly following up the collateral branch of the C . . . n-C . . . . l family resident in the United States.

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CENTRAL AREOLAR CHOROIDAL SCLEROSIS*
A HISTO-PATHOLOGICAL STUDY

BY

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THE history and clinical features of central areolar choroidal sclerosis—or atrophy, as designated by Nettleship (1884)—are recorded elsewhere in this issue (Sorsby and Crick, 1953). An affected member of one of the families described came to *post-mortem* examination, and the present study deals with the findings in this case.

Material

Mrs. Bertha C., aged 56 (CIII, 2 in Pedigree Chart II; Figs 5 and 6, pp. 130, 131). At the time of examination (June, 1949) her general health appeared to be good, but some 2½ years later she died shortly after an attack of coronary thrombosis. A *post-mortem* examination was performed by Dr. W. J. O'Donovan, who found the cause of death to be necrosis and fibrosis of the myocardium, atheromatous coronary occlusion, and hypertension. There was in addition severe atheroma of the thoracic and abdominal aorta, the internal carotids, and the basilar artery; the openings of the ophthalmic arteries were markedly narrowed by atheromatous plaques.

Technique of Histo-Pathological Study

Both eyes, together with the orbital contents, were removed at *post-mortem*. The branches of the ophthalmic arteries were dissected out and examined macroscopically.

Right Eye.—The specimen was irrigated with water and injected with Neoprene *via* the ophthalmic artery; the globe was opened transversely in order to examine the fundus. The cast of the choroidal vessels was then floated out of the eye, bleached with potassium permanganate and oxalic acid, examined microscopically, and photographed first in a glass sphere and subsequently as a flat preparation.

Left Eye.—After fixation in 10 per cent. formol saline the globe was opened horizontally and serial sections were cut through the affected area in the macular region, the following staining methods being used:

haematoxylin and eosin,
Mallory's triple stain,
Verhoeff's elastic stain and Masson's ponceau-fuchsin and light green,
PAS (Hotchkiss-McManus).

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Histo-Pathological Findings

Dissection of the vessels in the left and right orbital contents showed patchy atheroma of the ophthalmic artery, but the branches, including the posterior ciliary arteries, were relatively normal and no narrowing or occlusion was discovered at any point.

Injected Right Eye.—Only the larger arteries of the retina were injected and these showed no abnormality. A zone of retinal atrophy associated with an irregularity of the retinal surface extended from the macula to the disc margin. This area of retinal change corresponded exactly to a practically avascular circular area in the underlying choroid, which contrasted strongly with the remainder of the specimen in which the vessels were fully injected (Fig. 1). Microscopical examination of the choroidal cast showed that the chorio-capillaris was completely absent in the affected zone, and that, apart

FIG. 1.—Right eye. Neoprene cast of choroidal vessels mounted in a glass sphere. Compare with fundus drawing (*Fig. 5, p. 131*). *A well-demarcated avascular zone* extends from the submacular region to the disc. In the remainder of the specimen the vascular cast is complete.

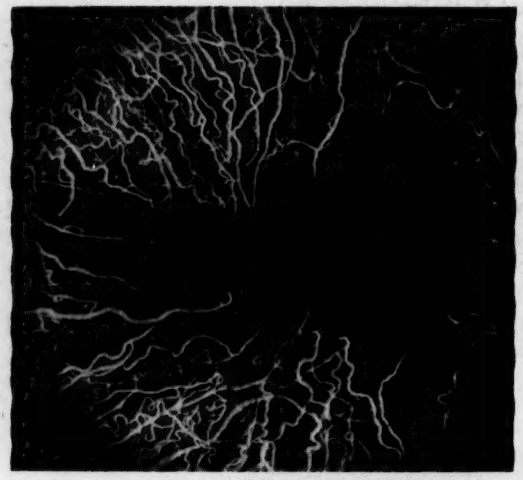

FIG. 2.—External view of Neoprene cast showing avascular zone extending from submacular region to disc. The area is well defined and, apart from the traversing ciliary arteries which have been severed at the sclera, only a few straggling atrophic vessels remain. The circle of Zinn around the optic disc is well shown.

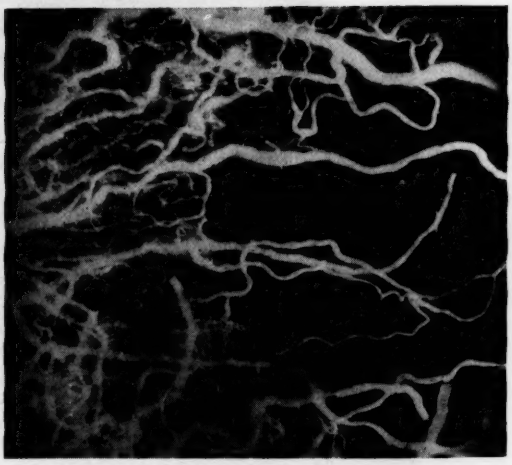

FIG. 3.—Internal high-power view of edge of atrophic area. The chorio-capillaris stops abruptly, providing the avascular area with a definite margin. Within the atrophic zone only traversing ciliary arteries and a few atrophied vessels may be seen.

from the traversing ciliary arteries which enter at this point, only a few straggling atrophic vessels remained to nourish the submacular choroid and the zone between the macula and the disc (Fig. 2). At the edge of the atrophic area the chorio-capillaris stopped abruptly, thus providing a well-demarcated margin to the avascular tissue (Fig. 3). The vascular architecture in the remainder of the choroid was apparently normal.

Sections of Left Eye.—The cornea, corneo-iridic angle, iris, and lens were normal. There was a mild degree of hyalinization in the ciliary body, and the choroidal stroma showed a moderate fibrosis and a scattered infiltration with Russell bodies, lymphocytes, and endothelioid cells. In

the macular region there was a remarkably well-demarcated zone of choroidal atrophy extending to the disc margin. Within this area the chorio-capillaris was almost completely absent and only a few patent vessels persisted in the fibrotic outer layers. The atrophied vasculature had left little trace of its previous existence, for, apart from a few shrunken vessels, it appeared to have merged imperceptibly with the fibrous stroma.

None of the vessels throughout the whole of the uvea showed even the slightest degree of sclerotic change; nor did the ciliary arteries, which could be seen both in their course through the sclera and extra-ocularly, show any abnormality.

Bruch's membrane showed no colloid bodies, and was apparently normal except in the macular region, where the underlying choroid was most markedly atrophic and avascular; here the membrane was somewhat less definite than elsewhere, showing a diffuse thickening and a patchy absorption of the elastic outer layer. None of the serial sections, however, showed any interruption in its continuity or any evidence of calcification.

Throughout the retina there were early *post-mortem* changes of cystic degeneration and incipient liquefaction of the rod and cone layer. The vessels appearing in the sections showed no arteriosclerotic changes. There was a *post-mortem* retinal detachment which was complete, except in the sharply localized area extending from the macula to the disc where the retina was lightly adherent to the underlying atrophic choroid. In this zone there was a correspondingly circumscribed loss of the outer layers of the retina, including the layer of rods and cones, the outer nuclear layer, and about half of the outer molecular layer; the inner nuclear layer, with a variable amount of the outer molecular layer intervening, had come to lie directly upon the choroid (Figs 4, 5, and 6, overleaf). The outer layers of the retina seemed to have vanished and there was no trace of glial replacement. Similarly, the pigment epithelial layer had also disappeared in this area and, apart from one small persistent island, there was no trace of either the epithelial cells or of their pigment. The optic nerve appeared normal and there was no abnormality in the vitreous or sclera.

Summary of Findings

(1) A well-demarcated avascular zone extending from the submacular region to the disc was present in the posterior choroid, as shown in the cast preparations.

(2) Histologically, this avascular zone was found to be atrophic and fibrosed. No arteriosclerotic changes were found either in the affected area or elsewhere in the choroid. Dissection of the posterior ciliary arteries failed to reveal constriction or occlusion.

(3) The outer layers of the retina together with the pigment epithelium had disappeared without glial replacement, in an area exactly corresponding to the underlying choroidal atrophy.

(4) Bruch's membrane was little affected by the failure of the choroidal blood supply.

FIG. 4.—Left eye. Section through affected area in macular region shows a fibrotic and practically avascular choroid. The outer layers of the retina have disappeared so that the inner nuclear layer lies directly upon Bruch's membrane, which appears little affected by the choroidal changes. Mallory's triple stain. × 100

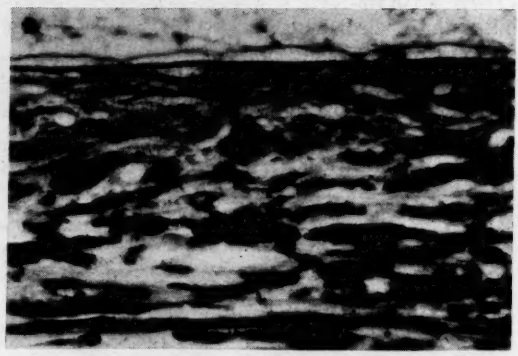

FIG. 5.—High-power view of fibrosed choroid in affected zone. Note almost complete absence of choriocapillaris and other vessels. Bruch's membrane appears normal, the pigment epithelium has disappeared, and the atrophic retina is lightly adherent to the choroid. There is no evidence of arteriosclerosis. Compare with Fig. 6. Mallory's triple stain. × 400

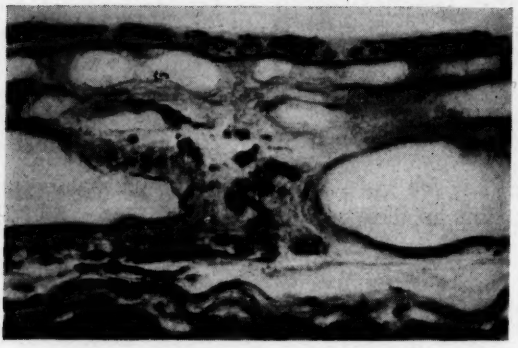

FIG. 6.—High-power view of equatorial choroid beyond affected zone. The vessels are normal in appearance and the pigment epithelium is intact; the overlying retina was detached due to artefact. Compare with Fig. 5. Mallory's triple stain. × 300.

Discussion

It would seem justifiable to assume that the disease, at least in its final stages, has a vascular basis. The pathological processes which may lead

to such a remarkably localized disappearance of the choroidal vessels may then be summarized as follows:

Vascular Occlusion.	Embolic, thrombotic, or arteriosclerotic.
Vascular Atrophy.	Primary: Heredo-degeneration.
	Secondary: To a selective toxic action or to a localized inflammatory process.

Vascular Occlusion.—If vascular occlusion is assumed, the well-circumscribed nature of the submacular choroidal degeneration would imply either a separate blood supply to this region or a peculiar vulnerability of the submacular vessels to disease. In connection with the first possibility, it has been suggested that the choroidal circulation is divided, either functionally or anatomically, into a series of terminal vascular systems. On clinical grounds there is strong evidence of such a sectorial arrangement, as was pointed out by Nettleship (1884) and Coats (1907), and particularly by Hepburn (1910, 1912) who concluded that there were three main sections of supply—the macular region, the mid-periphery, and the extreme periphery. That this is so, however, has never been conclusively shown anatomically, although Leber (1903) drew attention to the fact that the posterior ciliary arteries have but few branches of communication with each other, and that these occur mostly in the anterior part of the choroid and around the optic nerve entrance.

If such sectorial distribution exists, central areolar choroidal sclerosis might arise from occlusion of one of the short posterior ciliary arteries, either in the main trunk or in the perforating scleral branches, the retinal changes arising as a consequential ischaemic degeneration. Our findings in the sections and cast preparations would be in accord with such a possibility.

The insidious onset of the disease excludes an embolic or pure thrombotic process, but its occurrence in middle life or later would be in keeping with an arteriosclerotic vascular occlusion, and, in the case here reported, it would seem reasonable to link the choroidal lesion with the widespread arteriosclerotic changes found throughout the vessels elsewhere in the body. It was for this reason that a careful dissection of the posterior ciliary arteries in both orbits was carried out. Although patchy arteriosclerotic changes were found, no actual occlusion could be demonstrated, but any vessels so affected might well have disappeared or atrophied beyond macroscopical recognition. Nevertheless, the fact remains that examination of these eyes did not reveal involvement of the posterior ciliary arteries.

Arteriosclerotic involvement of the submacular choroidal vessels, as seen in secondary senile macular degeneration, must also be considered, especially since the fundus appearances in life were those generally attributed to choroidal angiosclerosis. A very complete study of serial sections of the left eye failed, however, to show evidence of arteriosclerotic changes within any of the intra-ocular vessels. Sclerosis of the choroidal vessels cannot, therefore, be accepted as an explanation of the choroidal changes in this particular case, and the view that central areolar choroidal sclerosis is simply an extension or severe form of a secondary macular degeneration (Klien, 1951) is not tenable in this instance.

Vascular Atrophy.—The assumption of a hereditary spontaneous atrophy affecting the submacular choroidal vessels, would have something to commend it, for such a process has already been held to be responsible for the disappearance

of the choroidal vessels in choroideremia and in gyrate atrophy; it would also fit in with the bilateral distribution and the familial incidence of the disease. On the other hand, choroidal atrophy in choroideremia and in the gyrate form occurs at a much earlier age, and tends to spread throughout the whole choroid; whereas the central areolar form remains localized and circumscribed. Nevertheless, it is well known that hereditary degenerations may be remarkably selective and, in the absence of a demonstrable choroidal or ciliary angiosclerosis, this explanation of a localized spontaneous atrophy remains an aetiological possibility, and gains some support from the fact that there was no evidence to suggest a selective toxic action or a localized inflammation as a cause of the vascular atrophy in this case.

The possibility that choroidal atrophy might arise from compression within the choroid must also be considered. As has recently been pointed out (Ashton, 1952), the choroidal vessels, lying within a fibrous stroma, are sufficiently confined by the intra-ocular pressure on the one side and by the sclera on the other for flattening of the veins to be caused at arterio-venous crossings. It would seem likely, therefore, that any further compression, such as may result from an intra-stromal leakage of blood or exudate, might well lead to collapse of the vascular bed within the affected area. Such a process would explain the well-defined zone of vascular atrophy in this case, but the histological material, showing only the end-stages of the disease, does not offer evidence to either support or deny such a concept.

The *post-mortem* examination of this material has, therefore, been disappointing in that it has not provided definite evidence of the pathogenesis of central areolar choroidal sclerosis. The only certain conclusion which can be reached is that the condition was not due, in this instance, despite the conflicting ophthalmoscopical appearances, to a choroidal angio-sclerosis. This, however, is an observation of considerable significance, for we have already called attention to this discrepancy between clinical and histological diagnosis in a case of fundus dystrophy (Ashton and Sorsby, 1951). The absence of any histological evidence of choroidal angio-sclerosis in these two different conditions, shows that the ophthalmoscopical appearance of opaque choroidal vessels does not necessarily imply an arteriosclerotic pathology. Alternative explanations must therefore be sought, and it is possible that such abnormal appearances may derive from perivascular exudates, from a localized exsanguinity of the vessels, or from fibrotic changes in the perivascular tissues. In any event the histological findings suggest that an ophthalmoscopical diagnosis of choroido-angiosclerosis cannot be made with certainty.

Role of Bruch's Membrane.—It is noteworthy that, in spite of the extreme avascularity of the submacular choroid, the overlying Bruch's membrane had remained intact and comparatively healthy. This apparent immunity to prolonged ischaemia is of importance in that the breaks in Bruch's membrane, which precede the development of angioid streaks (Böck, 1938; Hagedoorn, 1939; Klien, 1947; Verhoeff, 1948) and disciform degeneration (Brown, 1940; Verhoeff and Grossman, 1937), have been presumed by the workers quoted to be due to a deficient blood supply.

We have shown that dehiscences in Bruch's membrane were the fundamental pathological change in the case of fundus dystrophy previously examined (Ashton and Sorsby, 1951), and since arteriosclerosis was not a feature in this case, we

suggested that the breaks arose from a primary degeneration of the membrane. From this it followed that choroidal angio-sclerosis, when found in association with angioid streaks, disciform degeneration, or fundus dystrophy, was to be regarded rather as a parallel development than as a causative factor. While the case of fundus dystrophy provided evidence of pathological changes in Bruch's membrane without deprivation of blood supply, the present case of choroidal sclerosis further supports the above argument by providing an example of a grossly inadequate blood supply with no significant pathological changes in Bruch's membrane. In this connection it is interesting to note that Bruch's membrane was intact in the case reported by Klien (1951), although in that instance the choroidal angio-sclerosis was of sufficient severity to give rise to a secondary macular degeneration.

If the histology of this isolated case is indeed illustrative of the group of central areolar choroidal sclerosis as a whole, the absence of arteriosclerotic changes in the choroidal vessels suggests that the affection falls into the group of vascular atrophies rather than into that of the choroidal angio-scleroses.

Summary

The histo-pathological findings in a case of central senile choroidal sclerosis are reported.

In one eye, the well-demarcated avascular zone was demonstrated in a Neoprene cast of the choroidal vessels. Histological examination of the other eye showed the avascular zone to be atrophic and fibrosed, but no arteriosclerotic changes were found either in the affected area or elsewhere in the choroid. Dissection of the posterior ciliary arteries failed to reveal constriction or occlusion. The outer layers of the retina, together with the pigment layer, had disappeared without glial replacement in an area exactly corresponding to the underlying avascular choroid. Bruch's membrane was little affected by the failure of the choroidal blood supply.

The pathogenesis of the condition is discussed and it is concluded that the findings suggest a vascular atrophy rather than a choroidal angio-sclerosis.

My thanks are due to Professor Arnold Sorsby for provision of the material and to Dr. W. J. O'Donovan for the *post-mortem* report. I am indebted to Dr. Peter Hansell for the photographs, to Mr. A. McNeil for technical assistance, and to Miss E. FitzGerald for secretarial help.

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Brit. J. Ophthal. (1953) 37, 148.

SPECTRAL SENSITIVITY CURVES AND THE ABSORPTION OF LIGHT BY THE OCULAR MEDIA*

BY

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THE inter-relation of sensory, electrophysiological, and photochemical data in vision requires a knowledge of the behaviour of the retina in the absence of the ocular media. As far as the human eye is concerned, such knowledge is very inadequate in the case of the enucleated eye, and non-existent in that of the eye *in situ*. While light absorption by the pre-retinal and intra-retinal media cannot affect any mode of colour-vision, it modifies the sensitivity to light. The sensitivity of the eye to radiations of different wavelengths is usually defined as the reciprocal of the spectral energy required to produce a given constant sensation. It is immaterial whether the constancy means equality of brightness, threshold of vision, or absence of flicker; in all instances the experiment involves the measurement of energy. Since the photo-receptors are adjacent to the pigment epithelium, light reaching them must have travelled through the cornea, aqueous, lens, vitreous, and a major part of the retina proper. Every one of the structures acts as a light filter, thus reducing its intensity, and necessitating a larger supply of energy for the production of a given sensation than would otherwise be required. The energy is measured at the cornea. It follows that the sensitivity as measured at the cornea, S_W, is less than the receptoral sensitivity S_{REC} (Thomson, 1951). If the pre-receptoral structures were neutral, *i.e.*, if the percentage absorption of light were the same for all wavelengths, a knowledge of their characteristics would be important only in connection with measurements of the absolute sensitivity. All the scanty available evidence, however, indicates that they absorb selectively in different spectral regions (see Ludvigh and McCarthy, 1938, for data on human and animal eyes), the predominant absorption taking place at shorter wavelengths.

The unequivocal measurement of all the absorption characteristics in an intact human eye *in situ* is impossible. If enucleated eyes are used (Ludvigh and McCarthy, 1938), autopsy may mask the results, especially if the eyes are kept at 38° C., as should be done in all such cases. The application of animal data to human results is a doubtful remedy: in any case the intra-retinal absorption cannot be determined in this or in any other manner. This depressing outlook is somewhat mitigated by the circumstance that the spectral absorption of the pre-retinal media at long waves (green to red parts

* Received for publication October 27, 1952.

of the spectrum) is very nearly constant, so that in this region the shape of the spectral sensitivity curve as measured at the cornea agrees substantially with that of the receptoral sensitivity. This is deduced from a comparison between the human scotopic sensitivity curve and the absorption spectrum of visual purple (Wald, 1949). The pre-retinal media thus provide a convenient scape-goat for the wide discrepancies observed in the blue part of the spectrum for both photopic and scotopic sensitivity curves. These are usually ascribed to lens pigmentation or excessive macular pigment. The latter has occupied a key position in the question of pre-receptoral filters. Wald (1949) has measured the spectral absorption characteristics of human macular extracts, and found that they exhibited certain shape irregularities. Brindley and Willmer (1952) obtained a value for the macular absorption *in situ*, but the method is equivocal (Weale, 1953a).

However, while the first-order variations were of great interest a few years ago, recent measurements of the spectral sensitivity have focused the attention of visual physiologists on second-order effects, such as small inflexions and similar shape irregularities, superimposed on the general trend of the absorption curve. The reason for this is as follows:

The foveal photopic spectral sensitivity curve, measured with relatively large fields (Fig. 1*a*), subtending at the eye an angle of 1–2°, is smooth, with the exception of a slight modulation at short wavelengths (Thomson, 1949). But when the angular subtense is reduced to well below 1° (Fig. 1*b*), there appear secondary inflexions (Stiles and Crawford, 1933; Wright, 1946; Crozier, 1950; Thomson, 1951; Weale, 1951b) which are reproduced by most observers.

There arises the problem of the origin of these inflexions. Are the troughs (Fig. 1) caused by selective light absorption by pre-receptoral media, or are the peaks caused by an enhancement of the sensitivity in the relevant spectral region ?

The question why the mere reduction in the size of the test-field should produce filter effects which are absent when the field is large has never been squarely faced. Two of the inflexions (at 450 and 470 $m\mu$) appear, admittedly, also in large-field data (cf. Fig. 1*a*). Thomson (1951) failed to eliminate their counterparts in the small-field data by applying corrections corresponding to various amounts of macular pigment and Ludvigh and McCarthy's data for extra-retinal absorption. Moreover, such corrections, including one for haemoglobin, have only a small " smoothing-out " effect. The majority of the inflexions remain or become accentuated. Two facts have, therefore, to be admitted if the effects are wholly due to pre-receptoral filters: first, since large test-fields fail to detect the inflexions, the responsible filters must be concentrated nearly exclusively in the centre of the fovea, their extent subtending at the posterior nodal point an angle of less than 1°. Secondly, we are wholly ignorant of the spectral characteristics of such filters. The latter statement cannot surprise if the former is true. Assuming that the filters are present only in the central fovea, it is remarkable that they

should be found in that part of the human retina which is thinner than any other. Moreover, it is doubtful what function they should fulfil. Granted, as suggested by Dartnall and Thomson (1949), that a respiratory pigment is required for the foveal region because of the obstacles encountered in this region by the choroidal blood supply; the areal extent of such a pigment would have to exceed 1°. It would thus appear that the inflexions cannot be accounted for exclusively on the basis of local filtering actions.

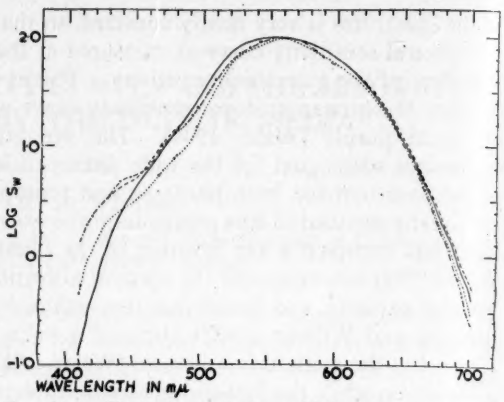

FIG. 1(*a*).—Photopic spectral sensitivity curves measured with a medium sized field (1-2°).

Full line: CIE;
dashed line: Gibson and Tyndall's mean value;
dotted line: observer L.C.T.;
dash-dot line: observer W.D.W.

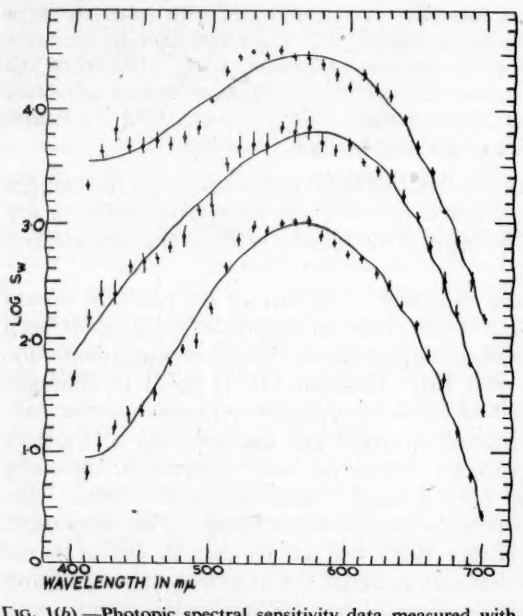

FIG. 1(*b*).—Photopic spectral sensitivity data measured with a small field (15-20′) in the foveal centre.

Full lines represent best-fitting calculated functions of the 4th degree (B.H.C.) and the 5th degree (W.D.W. and L.C.T.).
The vertical bars represent the standard errors of the mean.

In this and all other Figures the violet part of the spectrum is on the left, the red on the right.

Before the alternative is considered, namely that the irregularities superimposed on the general trend of the curves are due to a spectrally restricted receptor activity, it may be as well to assess their significance. Thomson (1951) and Weale (1951*b*, 1953b) have done so by fitting to the data orthogonal polynomials (Fisher and Yates, 1943). The basis of this procedure is that any continuous single-valued function $y = f(x)$ can be expressed as a power series:

$$y = a + bx + cx^2 + dx^3 \ldots (1)$$

The method of orthogonal polynomials consists in the determination of the co-

efficients *a*, *b*, *c*, etc. from known values of *y*. A perfect fit can always be obtained when the number of coefficients is equal to the number of values of *y*. In practice, the labour involved is unfeasible and unnecessary because the problem of photopic spectral sensitivity curves reduces to the question of whether or no a relatively simple expression, *i.e.*, one consisting of a few terms only, will describe all the experimental points to an accuracy comparable with that of the data themselves. When this was done for sensitivity curves (*y* was identified with log S and *x* with the wavelength λ), it was possible to evaluate the residual discrepancy Δ which was found to differ from zero in a statistically significant manner (Fig. 2). There are three regions in which Δ is positive: here the measured sensitivity is greater than would be expected if the experimental curve were smooth and single-humped.

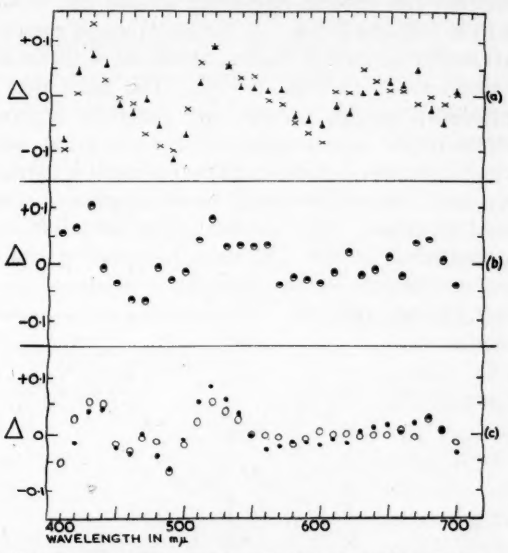

FIG. 2.—Δ, differences between experimental and calculated values (such as those shown in Fig. 1*b*) of log S_{11}.
(*a*) Two normal observers (15′ field),
(*b*) a protanope (15′ field),
(*c*) a cone-monochromat (O . . . 1° 20′ field, ● . . . 15′ field).
Note that there are three " humps " in (*a*) but only two in (*b*) and (*c*).

Moreover, the three regions are respectively located in the red, green, and violet parts of the spectrum, which has led to the suggestion that the three colour-mediating mechanisms, postulated by the tri-stimulus theory, add their weights to that of a dominant mechanism responsible for the perception of brightness. While the presence of the peaks and troughs in the spectral variation of Δ can be shown to prove that (1) is a function of a high order, no physiological significance can be ascribed to their spectral location.

Measurements of the photopic spectral sensitivity in the extra-foveal

regions throw further light on the possible origin of the shape irregularities and also on the contribution of light absorption by the macular pigment. The most remarkable feature of such measurements is the considerable increase in sensitivity to light of short wavelengths. This is illustrated in Fig. 3, where the foveal sensitivity is plotted side by side with the data obtained at a perimetric angle of 25° (Weale, 1953c). These values were obtained in the presence of a white surround which controlled the state of adaptation of a large part of the retina, the luminance level corresponding approximately to 1 *e.f.c.* both in the fovea and at 25°. The trends of the values of the sensitivity S_W, whose logarithm is plotted along the ordinate, are substantially alike between green and the long-wave end of the spectrum (520–660 mμ) but diverge considerably at shorter wavelengths. This difference means that the relative sensitivity at 440 mμ is about 15 times higher at 25° than it is in the fovea. A similar, though minor, increase has been observed at smaller perimetric angles, namely at 5° (Stiles and Crawford, 1933), and at 10 and 15° (Weale, 1951b). The facts that this increase continues at perimetric angles outside the generally accepted extent of macular pigmentation (10° surrounding the fixation area), and also that it depends on the luminance level at which the experiment is carried out (Fig. 4), render it unlikely that it can be due solely to the absence of macular pigment from those retinal locations. The indentation at 490–500 mμ has become much more pronounced in the 25° data, suggesting that the portion corresponding to wavelengths shorter than this is produced by a mechanism, particularly sensitive to spectral lights of this region.

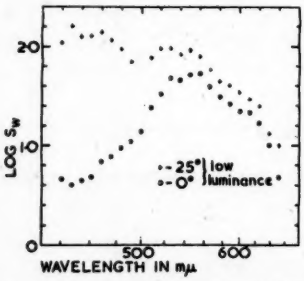

FIG. 3.—Comparison between photopic spectral sensitivities at the fovea and at a perimetric angle of 25°. Note vast relative increase in log S_W at short wavelength as periphery is reached.

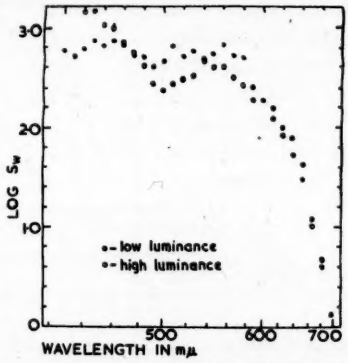

FIG. 4.—Comparison between photopic spectral sensitivities at 45°, measured at high and low luminance levels. Note how the latter gives rise to a flatter curve at short wavelengths.

The origin of the indentation observed in foveal sensitivity curves at about 600 mμ is indicated by a comparison of high luminance data (90 *e.f.c.*) obtained at 25 and 45° respectively (Fig. 5*a*). In these data, plotted for an equal quantum spectrum, pre-retinal absorption has been compensated.

The trough at 600 mμ might well be due to a pre-receptoral structure selectively absorbing in this region. It is shown in the fovea (Fig. 3) and in the 25° data at both luminance levels (Figs 3 and 5*a*). At 45°, however, though still present, the dent is much less pronounced. Moreover, the accuracy of the results is not much lower than that of the 25° data, so that the appreciable difference between the two curves cannot be ascribed to experimental errors. If an orthogonal polynomial of four terms (cf. equation 1) is calculated for the points between 499·7 and 681·4 mμ, the results given by the small black dots are obtained. The odds that all the residual deviations are due to experimental errors are about 100: 1 against. However, an inspection of the data reveals that the large deviation at $\lambda = 651{\cdot}7$ mμ and its small standard error greatly contribute to the heaviness of the odds against the calculated curve giving an adequate description of the experimental results. There is still no evidence against the belief that the hypothetical pigment absorbing mainly at 600 mμ should extend beyond a perimetric angle of 25° but not as far as 45°. Indeed, if enhanced sensitivities of two or more photochemical mechanisms are not responsible for the peaks on either side of this trough, the existence of such a locally restricted pigment in the retinal tissues must be postulated: if pre-retinal media were responsible and the applied correction

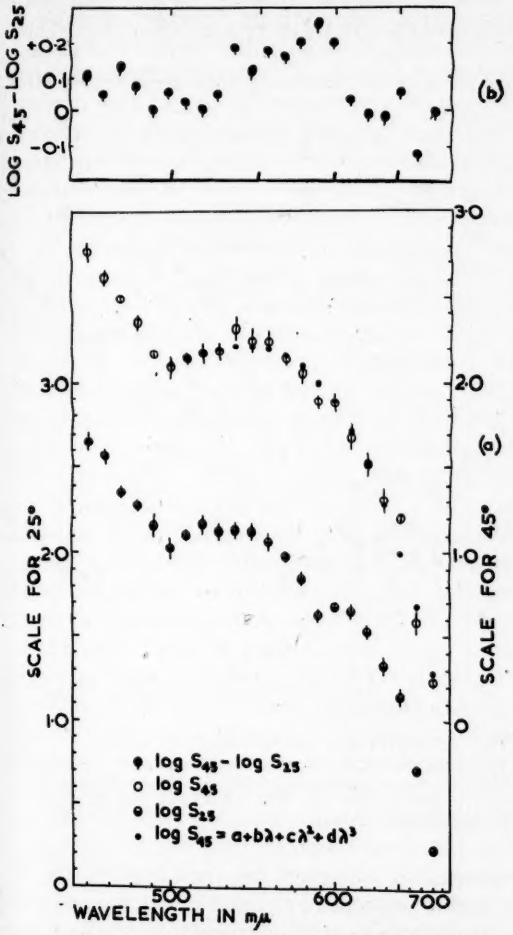

FIG. 5(*a*).—Comparison between photopic spectral sensitivity data at 25° and 45° corrected for pre-retinal absorption losses.

FIG. 5(*b*).—Log ratio (log S_{45}—log S_{25}) of (*a*) reveals a significant rise in sensitivity to light from yellow part of spectrum.

inadequate, the dent would have to appear to an equally marked extent at 45° also, unless their pigmentation is non-uniform.

It may be, of course, that after all this particular indentation is entirely due to an intra-retinal filter, and that the flattening observed at 45° is caused merely by a reduction in optical density, be it because the filter is becoming thinner or because the concentration of the pigment is reduced. The view that the disappearance of the irregularity is due to a modification of the photoreceptor system in the outer periphery is supported by a consideration of the wavelength discrimination data for these regions (Fig. 6). These were obtained in the usual manner by determining the just noticeable wavelength difference between two spectral lights under the same conditions as existed during the measurement of the spectral sensitivity, *i.e.*, the eye was adapted to similar luminance levels by means of a white surround (Weale, 1953c). Whereas the 25° measurements for both luminance levels exhibit trends characteristic of anomalous trichromatism, the data for 45 and 70° feature red-green confusion to a large extent: witness the large values of $\Delta\lambda$ between 500 and 600 mμ (when the ability to discriminate between lights of two adjacent wavelengths is poor, $\Delta\lambda$ is large and vice versa). Moreover, when the sensitivities for 25° and 45° are compared (Fig. 5*b*) a small but statistically significant increase is observed for the larger perimetric angle in this spectral region. If this fact is to be reconciled with the observed deterioration in wavelength discrimination, it must be postulated either that an independent peripheral mechanism, maximally sensitive to light of about 590 mμ, is adding its effect to that of the other mechanisms or that the " red " and " green " mechanisms, hypothesized by the tri-stimulus theory,

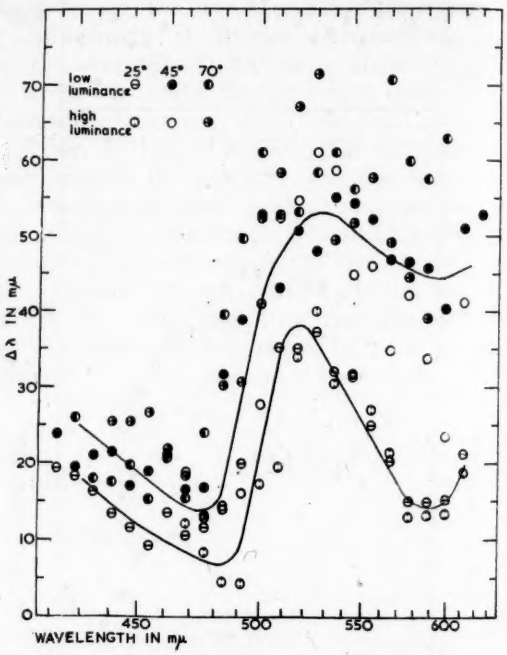

FIG. 6.—Wavelength discrimination in periphery. Note profound change in wavelength discrimination in region of 590–600 mμ as perimetric angle is increased from 25° to 45°. The curves are free-hand and merely serve to emphasize this change.

are being fused, or again that both the response curves representing the activity of these two mechanisms are reduced in amplitude and experience some broadening. When the relative increase in sensitivity to "blue" light is considered and it is borne in mind that this can be interpreted as a real reduction in the sensitivity of the "red" and "green" mechanisms, this third possibility appears to be the most plausible.

Although the above arguments indicate that some at least of the inflexions recurrent in the spectral sensitivity data of various observers are due to spectrally restricted enhancement in sensitivity, caused possibly by the presence of colour-mediating mechanisms, not all of them can be so explained. The outstanding example is afforded by the bifurcation of the humps in the central part of the spectrum (520–550 mμ). The evidence from data on wavelength discrimination that this, too, may be due to functional factors (Weale, 1951a) is slight. More convincing arguments are that the spectral location and the relative magnitudes of the prongs vary from one observer to another, and that they disappear with increasing field size.

Of the remaining inflexions, some appear only in isolated sensitivity curves. At the moment, no objective means can be envisaged which would determine whether they are due to individual differences in receptor mechanisms or to individual differences in pigmentation. One of the more promising lines of attack by subjective methods is spectral adaptation, which has so far been used only to a restricted extent (Wright, 1946). If adaptation by light of a wavelength at which the general trend of the curve shows a protuberance leads to its reduction, the enhancement must be due to functional factors. No data on this matter have yet been published.

The situation regarding the effect of the ocular media on the spectral sensitivity may therefore be summarized as follows. The foveal sensitivity curves for normal observers and for colour-defective observers of various kinds, measured with both small and medium size test-fields, consistently show two humps at about 450 and 480 mμ respectively. On the other hand, as the retinal area of measurement of the normal photopic sensitivity curve becomes more peripheral (10–70°), the curves obtained for a light-adapted eye exhibit an increase in sensitivity in these spectral regions. This cannot be due only to the absence of macular pigment from these retinal locations, since its total radial extent is approximately only 5° about the fixation area and the increase in sensitivity (relative to the long-wave regions) continues outside this limit. Moreover, the characteristics of Wald's macular extracts do not account for the inflexions found in the foveal curves. It can, therefore, be said with some confidence that the marked irregularities in this region are due both to selective pre-receptoral absorption and to a partial enhancement of the spectral sensitivity. The bifurcation observed in the medium wavelengths of the sensitivity curves of normal and colour-blind observers, while reported only in experiments carried out with fields smaller than 1°, persists in the peripheral data; there is some evidence, culled from results on

wavelength discrimination obtained at reduced luminance levels, to suggest that the twin peaks may be due to physiological rather than physical causes. But the presence of the bifurcation in the curves obtained for colour-deficient observers and for the normal light-adapted periphery suggests the opposite: the evidence is insufficient to decide which factor is responsible for this phenomenon.

Finally, the evidence that the dent at 600 mμ is due to the overlap of two photo-mechanisms is based on the facts that it is present in small-field data only, and that its gradual disappearance in the retinal periphery is accompanied by a deterioration in wavelength discrimination.

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OCULAR REACTION TO LENS PROTEIN*†
A PRELIMINARY STUDY

BY

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London

EXAMINATION of the literature on the subject of intra-ocular inflammation, with or without tension, arising as a result of the liberation of lens matter into the anterior segment, reveals the need for a careful review of the subject. Often tacit assumptions are made which appear to demand justification; conclusions are drawn from histological studies which have not been subjected to the critical analysis they deserve and demand; and a body of suspect theory has grown around the subject, whose very existence is queried in some quarters. It is for this reason that the matter has been taken up; a further stimulus was the striking fact that no writing on the subject emanating from Great Britain could be found, which appeared to indicate a justification for drawing attention to it.

Case Reports

Two of these patients were recently in the writer's care, and four were supplied in a personal communication from R. C. Davenport.

(1) Married female, aged 70. A left extracapsular cataract extraction, with peripheral iridectomy and anterior chamber washout, was performed in February, 1951. Recovery was quite uneventful and the patient left hospital after 10 days. Three weeks after operation her corrected vision was 6/6: no subsequent trouble was experienced.

In May, 1952, a similar operation was done on the right eye; some soft lens matter remained. Nine days later the eye was still very injected, with a "reactionary iritis"; the eye settled very slowly, and cortisone drops were used continuously. There was gross post-corneal deposit, and 7 weeks after operation a hypopyon appeared, and she was readmitted. Keratic precipitates were observed in the left eye. The eye whitened slowly under treatment, but 3 weeks later she showed a completely occluded pupil, iris bombé, and raised tension (44 mm. Hg Schiötz). An iris puncture was done and the eye settled slowly with normal tension. The right eye was still injected 3 months after the cataract operation and keratic precipitates were present in both eyes; the left showed a fine vitreous haze. Five months after the right cataract operation there were still keratic precipitates in each eye, more in the right eye than the left; vision was 6/6 in the left eye, and hand movements in the right with good projection.

(2) Married female, aged 69. A left extracapsular cataract extraction was performed in September, 1950. The patient was a diabetic subject, not taking insulin. She complained of some discomfort in the eye in May, 1951; the eye was slightly injected, one pillar was up to the wound, tension was normal; corrected vision was 6/24, probably attributable to retinal changes.

A right extracapsular extraction with peripheral iridectomy was done on July 31, 1952,

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† Dedicated to Professor Lindner on the occasion of his 70th birthday.

and on August 22 she showed bilateral injection, and heavy keratic precipitates in each eye with aqueous flare and cells ; the tension was full in the left eye. Corrected vision was 5/60 in the right eye and counting fingers in the left. She was admitted and treated with atropine, cortisone, and heat ; on discharge 12 days later there was slight residual injection of both eyes, post-corneal deposits, and a few cells in the aqueous. Corrected vision was 6/18 in the right eye and 6/36 in the left. Both eyes were white and quiet by September 23.

(3) Male, aged 68. A left extracapsular cataract extraction was performed on July 26, 1951, followed by an abscission of iris prolapse 3 days later. The patient was discharged on August 14 with a whitening eye, and in September his corrected vision was 6/18. A right extracapsular extraction followed in July, 1952, and he left hospital after 12 days. The tension was full (31 mm. Hg Schiötz) 6 weeks after the operation, with no flare. Two months after operation the right eye showed a heavy cellular deposit on the posterior corneal surface, with tension still full. The eye was settling slowly when last seen.

(4) Married female, aged 52, a high myope. She had a left extracapsular cataract extraction on August 29, 1946. Some iritis followed in October which necessitated re-admission for 2 weeks; atropine irritation was noted. The eye was white in December, and vision was subsequently 6/9.

A right extracapsular extraction followed on September 26, 1950, and the patient left hospital with an injected eye after 2 weeks. Heavy keratic precipitates were noted in December, 1950, the left eye being white. The tension then rose in the right eye, and she was admitted and a paracentesis was done on January 9, 1951. The eye was white in March, 1951. In November, 1952, she was awaiting right capsulotomy.

(5) Male, aged 69. A right extracapsular cataract extraction was performed on January 5, 1950, and the patient left hospital in 9 days with corrected vision 6/36. In March vision was $6/6_{(3)}$ in the right eye, and a capsulotomy was performed. On January 4, 1951, a left extracapsular cataract extraction was done. This was followed shortly after discharge in 9 days by a violent reaction which necessitated readmission for 2 weeks on January 20. Hyphaema and cells were present on the anterior chamber. On February 17 pus and keratic precipitates were present, and he was once again admitted. He was discharged with iris bombé and keratic precipitates, cells, and flare. He was later readmitted and an iridectomy was performed on July 12. His vision is now hand movements with good projection, and a Wheeler's iridotomy will probably be done later. The right eye has remained white with 6/5 corrected vision.

(6) Married female, aged 52, a high myope. A right intracapsular cataract extraction was performed on June 5, 1951; the capsule ruptured late and a small piece remained on the iris at 10 o'clock. On discharge 9 days after operation, vision was 6/18. The eye quietened rather slowly, and a few fine post-corneal deposits, with flare, persisted. In September the eye became painful, with full tension, corneal oedema, and many keratic precipitates; the left eye was a little injected with a few keratic precipitates. In January 1952, following cortisone treatment, she complained of much right-sided pain; the right eye was injected, with keratic precipitates, flare, and vitreous haze; the left eye was white. She was admitted to hospital for 6 weeks, when subconjunctival cortisone injections were continued. Atropine irritation was noted. A further period of in-patient treatment was given in July and August ; on discharge the right eye was quiet (vision 6/36), while in the left eye vision was perception of light with inaccurate projection. The left eye was injected, and showed a small hypopyon, many keratic precipitates, and a marked flare, tension being low. It is still irritable, and excision is to be carried out.

What is the condition with which one is dealing in the above cases? Is it one condition, or many, or variations of one condition? What features

distinguish it from sympathetic ophthalmia? What is the proper line of treatment and what can be done to prevent it?

These are questions which demand answers, and in the answer to the third lies a means of avoiding an experience which, though it comes seldom, none the less is so worrying that it is not easily forgotten.

The approaches to the problem differ considerably. As has been said, some deny the occurrence of an iritis or anterior uveitis as a manifestation of sensitivity to lens protein; others assume its existence without comment and discuss its treatment from this aspect; others again regard it as a mild form of sympathetic ophthalmia, or as a precursor of sympathetic ophthalmia. Yet again others regard a " reactionary " inflammation following cataract extraction as infective, or as due to the toxic action of lens proteins on the intra-ocular structures. It is proposed to discuss some relevant opinions and experiences; there would appear, incidentally, to be little doubt that into one of the categories to be thus discussed fall those cases of post-operative uveitis which in the past have been labelled as " mild " and " non-malignant " sympathetic ophthalmia, the lesion not being sufficiently intense or characteristic to justify enucleation and thus permit histological examination.

Courtney (1942) discusses " endophthalmitis . . . accompanying absorption of the crystalline lens ". A marked feature of the cases he describes is raised tension; all presented inflammatory reaction in the second eye following cataract extraction in the first eye after an interval varying from 3 months to 9 years; in some of these a spontaneous rupture of the lens capsule in the second eye was supposed to have occurred, or alternatively it is suggested that autolysed lens matter might have passed through the intact lens capsule. In one case Courtney concluded that the reaction in the second eye was caused by a sensitivity to lens proteins induced by the intradermal test. He concludes that, if one is satisfied that the endophthalmitis is due to absorption of lens proteins in the second eye after extra-capsular extraction of cataract in the first, the proper treatment, however intense the inflammation, is removal of all lens matter possible from the inflamed eye.

De Veer (1940) discusses endophthalmitis phaco-anaphylactica in its relation to sympathetic ophthalmia. He describes the three explanations of endophthalmitis after lens injury which have been given:

(*i*) It was first thought that the cause was infective, the lens matter providing a good bacterial medium. The possible importance of the synergistic action of bacterial antigens on lens protein antigen has been mentioned by several writers, and this aspect was stressed in the investigations of Cooper, Lakhani, and Javer (1948.)

(*ii*) The next suggestion was that of an inherent toxicity in retained lens matter.

(*iii*) Lastly Verhoeff and Lemoine (1922) produced the " anaphylactic theory ".

De Veer himself describes the histological characteristics of three eyes:

(*a*) One was excised 4 weeks after a preliminary iridectomy, when it was still acutely inflamed by iridocyclitis, and signs of sympathetic ophthalmia had appeared in the second eye. There was a mass of granulation tissue around the lens, and the capsule had been ruptured; the picture throughout the globe was characteristic of sympathetic ophthalmia.

(*b*) In the second case preliminary iridectomy on the right eye was accompanied by injury to the lens capsule. Extraction 2 months later was uneventful. A year later iridectomy was done on the left eye, and 2 months afterwards the cataract was extracted. Low-grade inflammation in this left eye followed ; the eye was soft when excised 4 months later, and 2 months later still the right eye was soft, with faulty projection. Again the histological picture was typical of sympathetic ophthalmia.

(*c*) The third case suffered an accidental knife injury, with damage to the lens, which was extracted 26 days afterwards. Both eyes were inflamed 3 months later, and the injured eye was excised. Inflammation in the sympathizing eye subsided gradually ; sections of the excised eye showed typical sympathetic ophthalmia.

De Veer concludes that endophthalmitis phaco-anaphylactica is to be regarded as a precursor of sympathetic ophthalmia, and cites these cases in proof, postulating a pre-existing sensitivity to lens protein. Criticism of these conclusions would appear to turn upon an agreed definition of the terms employed, and especially upon the histology of the anaphylactic condition. While the possibility of an allergic basis to the sympathetic phenomenon is generally admitted, it is difficult to see the justification for assuming that the lens protein reaction is to be regarded as the "precursor"—*i.e.* the cause—of a typical sympathetic ophthalmia as exemplified in those three cases.

Cooper, Lakhani, and Javer (1948) sought to investigate this type of inflammation by experiment with lens protein, paying regard to the possible activation of the antigen by staphylococcal or other toxin. They concluded that cases with a positive skin test before operation showed a benign post-operative course if they had been previously desensitized, and that desensitizing injections after inflammation had begun might have an adverse effect unless the dosage was very small. In a group of 132 cases, ninety were proved insensitive and developed no reaction after extracapsular extraction, and twenty-one were proved sensitive and developed post-operative inflammation; however, ten were insensitive and developed inflammation, and eleven were sensitive but remained quiet. There are so many variable factors in such a group that conclusions must be drawn with considerable reserve, and provision of controls is difficult. The writers have no doubt, however, of the existence of the condition of allergic inflammation due to lens protein sensitivity, nor of the value of pre-operative desensitization. They insist that such desensitization must be done with small non-increasing doses, and assert that increasing doses may actually sensitize a patient.

Irvine and Irvine (1952), reviewing the subject, produce cases which fit in to the three categories of response noted above, which they accept without comment. Much histological material is described, but the conclusions drawn from it are not always readily acceptable.

Present Investigations

In the hope that some aspects of this problem might be elucidated by further histological study it was decided to investigate sections of eyes removed on account of inflammation following extracapsular cataract extraction in all cases where the history suggested that they might provide relevant material. It was also hoped that some idea might be gained of the incidence

of this condition. The arbitrary period chosen was that during which the present writer was pathologist to Moorfields Hospital, *i.e.*, from October, 1933, to December, 1936.

Histological Material

During this period 1,402 specimens were sectioned and examined. Of these 416 were not eyes but portions of tissue, and there were thus 986 eyes to be considered ; the history and pathological aspects of all these were reviewed, and twenty were found that might provide important material relevant to the subject under discussion.

Thirteen were specimens of eyes removed for inflammatory trouble after cataract extraction from the first eye of a patient; these are referred to as " first eyes ".

Seven were specimens removed for similar reasons after cataract extraction in the second eye of a patient, following a similar previous extraction in the first eye; these are referred to as " second eyes ".

All twenty specimens were re-examined under the microscope, numbered for reference purposes, and grouped according to the findings.

First Eyes (Nos 1 to 6).—These were all rejected on the grounds that they did not appear for various reasons on histological examination to fall into the category under consideration.

No. 1 was removed 2 months after extraction, and showed much inflammatory reaction and total detachment of the retina.

No. 2 showed panophthalmitis with vascularized granulation tissue occupying most of the anterior segment, and a degenerate, haemorrhagic, sloughing retina.

No. 3 showed a typical secondary glaucoma with little inflammatory reaction, the iris being adherent to the cornea.

No. 4 suffered an abscission of a prolapsed iris the day after extraction; an acute iridocyclitis supervened, tension was low, and there was retinal perivascular cuffing and choroidal infiltration, with no inflammatory reaction around the lens remnants—a probable early sympathetic ophthalmia.

No. 5 showed similarly low tension, with a total detachment of the retina.

No. 6, one year after a successful extraction with resulting 6/9 vision, showed high tension of a haemorrhagic type.

First Eyes (Nos 7 to 13).—These all appeared to provide material which would prove valuable in the consideration of this group.

No. 7 was a scoop extraction with vitreous loss; the capsule was separated from the wound 11 days after extraction. The eye was painful and showed keratic precipitates 5 months after operation: sections showed intense inflammatory reaction around the lens remnants.

No. 8. A large piece of nucleus was left lying on the ciliary body; inflammation with keratic precipitates followed and the eye was excised. A condition of endophthalmitis was present, the lens remnants being surrounded by inflammatory tissue.

No. 9 was excised a year after extraction; iritis and secondary glaucoma were present, the lens remnants being similarly surrounded and infiltrated by inflammatory cells.

No. 10. A similar interval passed between extraction and enucleation; post-inflammatory atrophy of the uvea was marked, and eosinophiles were present in the atrophic tissues.

No. 11. The reaction was mild only, though some inflammatory cells were present amongst the lens remnants.

Nos 12 and 13. Reaction was intense; excision was done 4 and 3 months respectively after extraction, and the lens remnants were copiously invaded by inflammatory cells.

Second Eyes (Nos 14 to 18).—These five specimens were rejected as irrelevant because of many complicating factors.

No. 14 was from a diabetic patient, whose second eye became painful, with cataract and secondary glaucoma, 9 years after cataract extraction from the first. Paracentesis failed to relieve the tension, and the iris prolapsed through the operation wound.

No. 15 showed a right detachment and left macular degeneration as well as lamellar cataracts. Left preliminary iridectomy was followed by extraction in 1929, and right extraction was done in 1930; pain led to right enucleation in 1935.

No. 16. Left extraction was followed a year later by pain in the right eye with keratic precipitates and raised tension; the interval was considered to be too long to allow inclusion in the series, though admittedly the histological picture differed little from that seen in many included cases.

No. 17. The history was too defective to permit inclusion.

No. 18 had had left extraction in April, 1925, followed by capsulotomy in August. In January 1926, the right eye was injected, with hypopyon, cataract, and high tension; there was no perception of light. On section, the anterior segment showed only mild inflammation; there were exudate and cells in the anterior chamber but no keratic precipitates. Retina and choroid showed no involvement; the cataract was Morgagnian, with an intact capsule, and was of course not invaded by cells.

In the light of later experience it may prove to be that it would have been more correct to include this last case.

Second Eyes (Nos 19 and 20).—These two specimens give histological evidence of the correctness of their inclusion in this group.

No. 19. A right cataract extraction was followed by iridocyclitis and the eye was "excised too late". The trouble in the left eye was diagnosed as sympathetic ophthalmia; the section showed a picture not suggestive of sympathetic, but the interesting feature was that the lens capsule was incomplete, and inflammatory cells had invaded the lens; an intense plastic iridocyclitis was present. This may well be a most important case in view of Courtney's theories.

No. 20. A right cataract extraction was followed 2 years later by a glaucoma iridectomy in the left; 2 years later the left eye was blind, with keratic precipitates and low tension, while vision in the right eye was 6/9. The section showed an iridocyclitis, with ruptured lens capsule and intense inflammatory invasion of the lens.

Discussion

No one is more conscious than the writer of the difficulty of drawing correct conclusions from the evidence contained in the foregoing—historical, clinical, and histological—nor indeed of the fatal ease with which unjustified or even frankly incorrect conclusions could be drawn.

The study of this condition would be simplified if it were restricted to the occurrence of inflammation in a second eye subjected to extracapsular extraction following a similar operation in the first. But such an approach would entail an unjustifiable over-simplification. One is compelled to consider the possibility that a given patient may be inherently sensitive to lens proteins, a state of affairs which leads to reactionary inflammation after release of the proteins in a first eye. Again, spontaneous rupture of the lens capsule is postulated, and it must be admitted that this theory receives some histological support in the series examined. Further, reference to the literature leads one to consider the possibility of the passage of autolysed lens matter through the intact capsule ; this suggestion opens the door wider still.

While doubts of the occurrence of a phaco-anaphylactic response are still expressed in some quarters, it is clear that the majority of writers on this and allied subjects are convinced of its occurrence.

The clinical evidence submitted seems to go a long way towards supporting this view. At least one may say that the cases quoted may be satisfactorily and completely explained on the hypothesis suggested—that they "fit in" with the theory, and that no more attractive theory presents itself.

One might consider that the weightiest evidence might be derived from histological studies, but it is just here that the greatest difficulties of interpretation arise. It is by no means certain that the presence of inflammatory invasion of the lens remnants in an eye subjected to extracapsular extraction indicates that the inflammatory reaction which led to excision was caused by any abnormal sensitivity to lens proteins on the part of the patient. Eyes are undoubtedly lost through simple " post-operative inflammation "—most likely an exogenous invasion. Again, in every instance recorded here, the reaction found in a " first eye " following extracapsular extraction presupposes a natural or inherent sensitivity to such proteins ; is this truly an in-dwelling sensitivity, or was it induced by previous transudation of the products of lens autolysis through an intact capsule—a process which set the stage for a violent reaction when the lens matter was liberated by operation?

Any error in sifting the histological evidence examined here has been in rejecting sections which might possibly have lent support to the hypothesis of lens sensitivity. There is no doubt that eyes which have been excised on the clinical suspicion of sympathetic ophthalmia have in many instances proved histologically innocent, and the very attractive alternative of phaco-anaphylaxis is difficult to reject.

It is clear that further research in this subject is urgently demanded. From the present study it is difficult to escape the conclusion that phaco-anaphylaxis is a real occurrence ; what is needed is more knowledge of the clinical differentiation between this and a mild or early sympathetic ophthalmia, for upon this depends the fate of the inflamed eye. The problem is infinitely more difficult if, as de Veer suggests, a sensitivity to lens protein is to be regarded as a precursor and primary cause of sympathetic ophthalmia. It is intended to follow this preliminary study by further investigation especially on the histological side. It is essential to discover what support there is for the separation of the phenomena of the ocular response to lens proteins into three categories : phaco-anaphylactic, toxic, and phacogenetic (it must be admitted that this last title stands condemned at the outset on etymological grounds). If one is satisfied of the existence of an allergic response, a decision must be made on the question whether patients are to be subdivided into four types :

(*i*) those inherently sensitive to liberated lens protein;
(*ii*) those not so sensitive;
(*iii*) those in whom liberation of lens protein in one eye brings about a sensitization which causes a violent reaction to the subsequent liberation of lens protein in the second eye;
(*iv*) those in whom it does not.

Spontaneous rupture of the lens capsule, " microscopic dehiscences " of the capsule (Irvine and Irvine 1952), and transudation of autolysed lens matter through an intact capsule, are all conceptions complicating the issue and increasing the difficulty of classification. An attempt will be made to correlate clinical findings with histological appearances, and in particular

to investigate the general significance of the invasion of lens matter by inflammatory cells and the special significance of the specific nature of these cells.

The most productive line of clinical research would seem to be an extension of the work of Cooper and others (1948), by attempting to discover whether a patient is sensitive to lens protein injection, with a careful subsequent study of the effect of extracapsular extraction. The result of such an investigation should show whether a pre-operative sensitivity test is justifiable or valuable, and whether, if the results are positive, pre-operative desensitization should be undertaken.

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QUANTITATIVE STUDY OF VISUAL AFTER-IMAGES*

BY

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MUCH has been written on the persistence of visual sensation after the light stimulus has been removed—the so-called visual after-image (Helmholtz, 1924 ; Duke-Elder, 1932). The after-image may be positive, in which the light and dark parts correspond to those of the object, or negative, in which the light and dark parts are reversed. Similarly, in the positive after-image of a coloured object, the colours roughly correspond to those of the object, whereas in the negative after-image complementary colours are said to appear.

With a very bright stimulus, the after-image may persist for several minutes or perhaps longer, whereas under more normal conditions the duration is short, and may be studied by experiments on flicker and persistence of vision. Whilst the short-period phenomena have received considerable attention, the long-period after-images have mainly been studied qualitatively, and no comprehensive quantitative experimental work appears to have been done.

Craik (1940), and later Cibis and Nothdurft (1948), have described experiments from which they conclude that after-images are of retinal origin, and Misiak and Lozito (1951) show that some central modification of after-images occurs. To decide, however, on the mechanism of after-images, and on their relation to other phenomena of vision seems premature until more experimental data is available. Pannevis (1947; 1948) has made measurements on the brightness variation of long-period after-images, although the amount of work is not great. His method was to re-stimulate the retina and induce a negative after-image equal in apparent brightness to the positive after-image, so that no resultant image could be seen. The assumption that the positive after-image is not affected by re-stimulation is probably unjustifiable. Probably the reason for the lack of adequate quantitative data is due to the difficulty of evolving a technique for making adequate measurements.

The author has found that, by using the binocular matching technique of Wright (1946), measurements could be made of the retinal illumination of one eye which caused a sensation of brightness equal to that of the positive after-image in the other eye. Also he has found that by taking a sufficient number of observations, significant quantitative data can be obtained.

Work has been done with white light† stimuli only, on a dark-adapted eye.

* Received for publication November 3, 1952.

† Colour temperature 2900°K.

The comparison matching stimulus was also white, but no great difficulty was experienced since the after-images were only slightly coloured, and this colouration could be ignored. Measurements could only be made of positive after-images, but since negative after-images are usually caused by re-stimulation, they did not appear under the conditions of the experiments.

Method

The apparatus (Fig. 1) consists of two similar optical systems. The first provides the stimulus for the left eye. Light from a line-filament lamp S_1 is collimated by lens L_1. A photographic shutter E used for timing the exposure to the stimulus, and a neutral density filter F_1 for varying the luminance of the stimulus, are placed in the parallel beam of light. The diaphragm B_1 defines the image field, and has a rectangular opening subtending an angle of $2° \times 1°$ at the eye. This diaphragm is in the first focal plane of the lens L_2, and can thus be viewed by the unaccommodated eye. A pinhole A_1 (1 mm. diameter) is placed in the second focal plane of L_2, and thus the light passing into the eye must have passed through B_1 parallel to the axis.

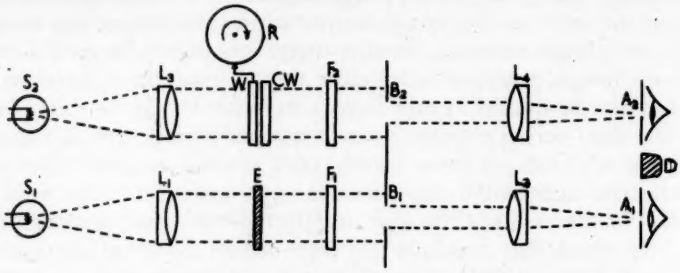

FIG. 1.—Apparatus.

The second system provides the comparison field of variable luminance for the right eye. It is similar to the first, except that the diaphragm B_2 provides a $2° \times 1°$ rectangular comparison field which appears slightly above the stimulus field, when they are viewed binocularly. This is in order that the two fields shall not be fused. The luminance of the comparison field can be varied by rotating a knob which moves a logarithmic photometric wedge W. In order to provide a uniform field luminance a fixed compensating wedge CW is used. The range of luminance can be changed by introducing neutral density filters at F_2. The position of the wedge W is a measure of the luminance of the comparison field, and thus (since a constant pupil is used) of the retinal illumination, and this is recorded continuously on a drum R which is rotated by a synchronous electric motor. The instrument is calibrated in retinal illumination by matching the apparent brightness of a white diffusing test surface within the instrument, with that of the field of the instrument. The white diffusing surface is illuminated by a standard lamp at a known distance, and thus its luminance can be calculated. The retinal illumination is calculated from the luminance and the pupil area. The position of the observer's head is rigidly fixed by a dental impression D.

After a period of dark-adaptation the left eye is stimulated by opening the shutter E. Four red fixation dots are provided at the four corners of the rectangular stimulating patch before the exposure, in order that the stimulus should always affect the same area of the retina. These fixation dots are extinguished immediately after the end of the stimulus. The position of the wedge is then continually adjusted to maintain equality of sensation of brightness between the comparison patch and the after-image.

Results

Owing to the difficulties of the technique and the large number of observations needed to obtain significant results, all the results are those of one observer, the author. It was thought that detailed results from one observer would be more valuable than less detailed results from a number of observers.

The first experiments were concerned with the effect upon the after-images of the period of dark-adaptation of the eye. It was found by experiments performed with the eye dark-adapted for times varying from 5 to 30 minutes that little difference in the after-image occurred after an adaptation time of 10 minutes. All the subsequent experiments were carried out with 10 minutes dark-adaptation. The interval between separate experiments was never less than half an hour, and during this time the eye was exposed to light and then dark-adapted again. This ensured that faint after-images did not affect the next experiment.

Experiments were next carried out on the reproducibility of the results. Figures 2(*a*) to 2(*h*) show actual curves from the apparatus of log. of the retinal illumination in trolands* (R) of the right eye which causes a sensation of brightness which balances the after-image sensation in the left eye, plotted against the time (*t*) in seconds which has elapsed from the beginning of the stimulus. The stimulus producing the after-image was a retinal illumination of 2,000,000 trolands for one second. The curves show eight separate determinations, the eye having been dark-adapted for 10 minutes before each experiment. It was found that the mean-ordinate curve of eight separate determinations yielded a curve which was consistently reproducible for the same exposure conditions. This mean curve is shown in Fig. 3.

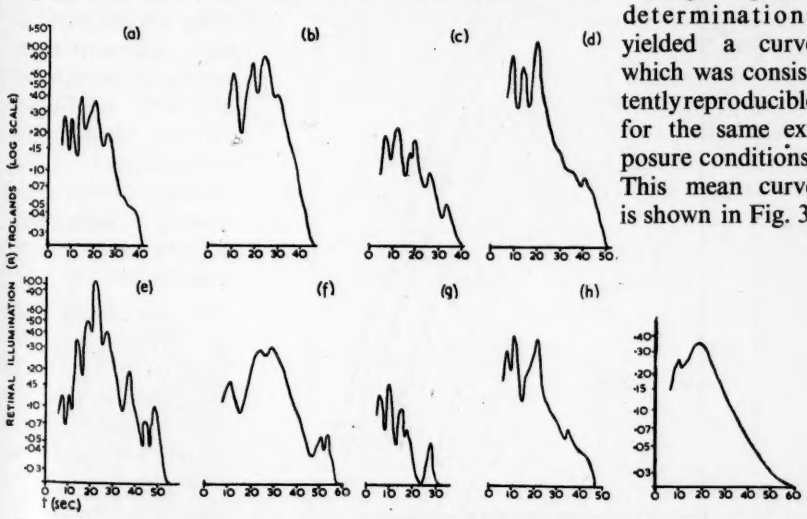

FIG. 2.—After-images produced by a stimulus of 2,000,000 trolands for 1 sec.

FIG. 3.—Mean-ordinate of curves in Fig. 2.

* The retinal illumination is 1 troland when a surface of luminance 1 candel/sq. m. is viewed through a pupil of area 1 sq. mm.

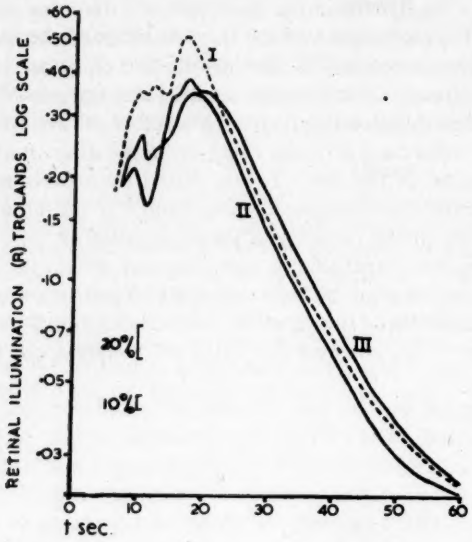

FIG. 4.—Mean-ordinate curves for three separate determinations.

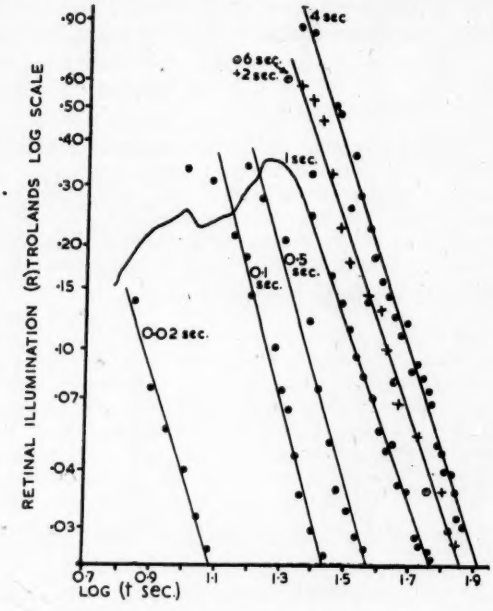

FIG. 5.—After-images produced by a stimulus of 2,000,000 trolands for various exposure times.

In order to ascertain whether the reproducibility was maintained over a long period, the eight experiments were repeated three times, with an interval of three months between the first and second, and of one month between the second and the third. The mean curves from these three experiments are shown as curves I, II, and III in Fig. 4. The ordinate intervals corresponding to a variation of retinal illumination of 10 and 20 per cent. are shown. The total variation between these curves is mostly of the order of 20 per cent. in retinal illumination. This consistency was considered sufficiently high to justify further experiments.

It was found that by plotting log. R against log. *t* an approximate straight line resulted. These graphs are shown in Fig. 5 for after-images produced by a stimulus of retinal illumination 2,000,000 trolands. The time of

exposure to the stimulus is indicated on each curve. The 1-second curve, which is shown in full, was the mean of 24 determinations. The decay parts only of the other curves are shown, and each is the mean of eight determinations. The points used for the log. log. plots are taken at arbitrary intervals from the experimental curves.

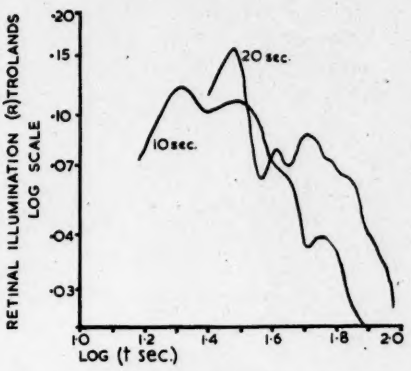

FIG. 6.—After-images produced by a stimulus of 2,000,000 trolands for 10 and 20 sec.

It can be seen that the sensation of brightness and duration of the after-image increases up to 4 seconds exposure. With longer exposures the after-image is fainter and less persistent; the after-images produced by a 2-second and a 6-second exposure are practically identical. With still longer exposures linearity no longer exists. Curves for 10- and 20-second exposures are shown in Fig. 6.

The mean gradient of the straight lines shown in Fig. 5 is about —3.0. This suggests that the decay part of the variation can be represented approximately by the relation log. R = —3 log. t + c, where c is a constant; we thus have $R \alpha t^{-3}$. Pannevis (1947; 1948) obtained similar straight lines in some experiments, although his experimental method was quite different, and hence his results cannot be compared with those of the author.

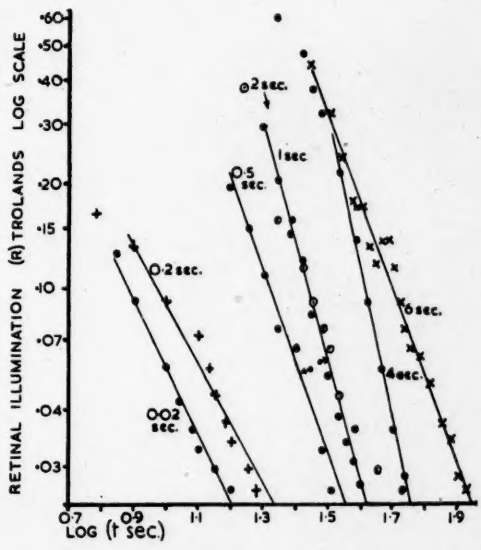

FIG. 7.—After-images produced by a stimulus of 1,200,000 trolands for various exposure times.

Fig. 7 shows a similar series of graphs for after-images produced by a less intense stimulus of retinal illumination 1,200,000 trolands. These results are less consistent than with the more intense stimulus. The mean gradient is —2.8, giving an approximate relation $R \propto t^{-2.8}$ for the decay part of the curves.

No theory is suggested to explain these results since it is considered premature until more data are acquired. It is intended to extend this work to obtain information for after-images produced by monochromatic stimuli throughout the visible spectrum.

The work does show, however, that significant quantitative measurements on positive after-images can be obtained by using Wright's binocular matching technique.

Summary

Wright's binocular matching technique has been applied to the quantitative study of positive visual after-images. The sensation of brightness of the after-image in one eye is balanced binocularly by the sensation caused by a comparison light stimulus in the other eye. It is shown that by using this technique significant quantitative measurements can be obtained.

The author wishes gratefully to acknowledge the help and advice throughout this work of Professor W. D. Wright and Mr. F. Y. Poynton. He also wishes to thank Mr. H. Matthews for his help in the design and construction of the apparatus.

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MANDIBULO-FACIAL DYSOSTOSIS*

BY

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THE first recorded cases of this comparatively rare congenital anomaly were reported by Berry (1889), but it was not until 11 years later that Collins (1900) recognized that the condition occurred as a syndrome. Further cases in Great Britain have been described by Mann and Kilner (1943) and Johnstone (1943). The clinical picture varies considerably from case to case and atypical, incomplete and unilateral forms may occur. It has been described under various names, in England as " Treacher Collins' Syndrome ", and on the continent of Europe as the " Syndrome of Franceschetti ".

The original cases described by Berry (1889) comprised a mother, her brother, and her daughter, who all shewed obliquity of the palpebral fissures, colobomata of the eyelids, and defective development of the chin (micrognathia) ; these are now classified as abortive forms of the full syndrome.

Collins (1900) and Tyrrell (1903) described in addition flattening of the cheeks due to hypoplasia of the malar bones. McMullen (1920) described a unilateral case, and Pires de Lima and Monteiro (1923) first described the fully developed syndrome. Numerous case reports followed—Isakowitz (1927), Waardenburg (1932, 1934), Hermans (1936), Van Lint and Hennebert (1936), Kazanjian (1936), McEnery and Brennemann (1937), Debusmann (1940), Sanvenero-Rosselli (1940, 1948), Mann and Kilner (1943), Johnstone (1943), Franceschetti and Zwahlen (1944), Leopold, Mahoney and Price (1945), Schachter (1947), Brohm and Kluska (1947), Holm (1948), Brégeat and Naud (1949), Waardenburg (1948), Navis (1948), Straith and Lewis (1949), Labourcarie and Gayral (1949), O'Connor and Conway (1949), Halberg and Paunessa (1949), and Streiff (1950).

The fully developed syndrome consists of certain associated congenital and familial deformities of the ears, malar bones, lips, chin, and lower eyelids. The general similarity in appearance of the affected patients is very striking, although the number and extent of the deformities (which are usually bilateral) vary considerably. The appearance is unmistakable and the face has a characteristic fish-like aspect. The main features (see Table of selected cases) are :

(1) An anti-mongoloid obliquity of the palpebral fissures, sometimes associated with colobomata of the outer portion of the lids (usually the lower lids).

* Received for publication October 23, 1952.

TABLE

SUMMARY OF SELECTED CASES OF TREACHER

Author		Date	Malar Eminence	Lower Orbital Margin	Palpebral Fissure	Axis of Eyeball	Lower Eyelids
Treacher Collins	(1)	1900	Flattened	Deficient	Oblique (downward laterally)	?	Bilateral notches
	(2)	1900	Flattened	Deficient	?	?	Unilateral notch
Mann and Kilner	(1)	1943	Flattened	Deficient	Oblique	Normal	Thin and atrophic
	(2)	1943	Flattened	Deficient	Oblique	Normal	Bilateral notches
Straith and Lewis	(1)	1949	Flattened	Deficient	Oblique	Normal	Bilateral notches
	(2)	1949	Flattened	Deficient	Oblique	Oblique	Bilateral notches
	(3)	1949	Flattened	Deficient	Oblique	Normal	Bilateral notches
	(4)	1949	Flattened	Deficient	Oblique	Oblique	Bilateral notches
	(5)	1949	Flattened	Deficient	Oblique	Normal	Normal
Present Author		1953	Flattened	Deficient	Slightly oblique	Normal	Normal

* Two cases reported by Berry (1889) had only the

(2) Hypoplasia of the facial bones, especially the malar bones, the zygomatic arch and the mandible, resulting in flattening of the cheeks and recession of the chin (micrognathia).

(3) Malformation of the external ears, sometimes involving the middle and internal ears with consequent impairment of hearing. The auricles are placed lower than the normal position, and point backwards. Auricular fistulae may be present.

(4) Deformities of the lips and mouth; the lip and palate may be cleft; the palate tends to be high and arched, with malocclusion of the teeth, and the upper lip may be enlarged with macrostomia.

(5) The chief associated deformities are:

(*a*) Blind fistulae between the angles of the mouth and the ears.

(*b*) Tongue-shaped projections of the hair line on to the cheeks.

(*c*) Atrophy of the medial portions of the lower lids, with absence of the lashes and Meibomian glands over the affected area. The puncta may be absent: the naso-lacrimal ducts may be obstructed.

COLLINS SYNDROME REPORTED IN THE LITERATURE*

Eyelashes (Medial ⅓ Lower Eyelid)	External Ear	External Auditory Meatus	Hearing	Maxilla	Mandible	Other Abnormalities
?	Normal	Normal	Normal	Narrow	Receding chin	?
?	Normal	Normal	Normal	?	?	?
Bilaterally absent	Normal	Normal	Deaf	High, narrow Prominent front teeth	Receding chin	None
Collection of lashes at distance to lateral commisure	Bilaterally deformed	Absent	Deaf	High, narrow	Receding chin	Cleft palate
Absent medial ⅓ right lower lid	Slightly deformed bilaterally	Deficiency of helix laterally	Partially deaf	High, narrow Prominent front teeth	Receding chin	Long second metatarsal bone
Normal	Bilaterally deformed	Absent	Deaf	High, narrow Prominent front teeth	Receding chin	Long second metatarsal bone Flat parieto-occipital skull
Absent right, sparse left	Bilaterally deformed	Unilaterally absent	Unilateral deafness	Prominent upper front teeth	Receding chin	Long second metatarsal bone Flat, parieto-occipital skull Hypermotility in metatarso-phalangeal joints
Bilaterally absent	Bilaterally deformed	Normal	Normal	High, narrow Prominent front teeth	Receding chin	Long second metatarsal bone Hypermotility in metatarso-phalangeal joints
Bilaterally absent	Bilaterally deformed	Normal	Normal	High, narrow Prominent teeth	Receding chin	As above
Present	Bilaterally deformed	Very narrow overhanging superficially	Unilateral partial deafness	High, narrow Prominent front teeth	Receding chin	Webbed second and third digits of both feet Lacrimal puncta present

deficient lower eyelids and are not included.

(*d*) Flattened parieto-occipital bones.

(*e*) Nasal deformities.

(*f*) Skeletal deformities, such as long second metatarsal bones, club foot, and hypermotility of the metatarso-phalangeal joints.

The hereditary character of the syndrome has been established by numerous genealogies reported in the literature (Debusmann, 1940; Leopold, Mahoney, and Price, 1945; Brohm and Kluska, 1947). Cases appear to occur more frequently in the lower social and economic grades, and it has been suggested that advancing age in the mother (and possibly deficiencies in her diet) may be among the causative factors. The aetiology of the condition is clearly genetic, and defective ossification of the bones of the face, derived from the visceral mesoderm, provides the primary lesion. The defect must presumably date from about the seventh week of foetal life. Similar anomalies have been produced in chicks by *x* irradiation during development (Wolff, 1934). Treatment of the defects involves plastic procedures to raise the level of the outer canthus in severe cases. Cartilage implants may be desirable to alter the contour of the face and various forms of plastic operation may be required to remedy the position and shape of the ears.

Case Report

A boy aged 10 was originally presented for treatment with a history of inflammation and discharge from both eyes over a period of several years. His facial appearance had been abnormal from birth, but there was no family history of facial or other congenital abnormalities. He had been noted to be a mouth-breather and his mouth had always been deformed. Articulation was satisfactory. There was some deafness of the right ear but he was making satisfactory progress at school. His general appearance was that of mandibulo-facial dysostosis, although the eyelids did not show bilateral notching. There was deficiency of both malar bones and noticeable flattening in the region of the infra-orbital ridges. Cilia were present throughout the lower lids but on both sides there was lacrimal obstruction, with copious muco-purulent regurgitation from the lacrimal sacs and some associated chronic conjunctivitis. The chin was small and receding and there were bilateral deformities of the external ears, which were caudal to the normal position, pointing backwards and upwards. There was a supra-auricular fistula on the right side (which was still discharging) with a scar in a similar position on the left side, and some scarring down the anterior borders of the sterno-mastoids. The palate was high and narrow: the nose showed a broadened, enlarged bridge : the external auditory meatuses were present but very narrow and overhanging superficially : the upper lip showed the presence of a fairly extensive lymphangioma, with considerable deformity (see Figs 1, 2, and 3).

Eyes.—Apart from the condition of the lacrimal apparatus and the associated conjunctivitis, both eyes were normal externally, the pupils equal and active, the media clear and the fundi normal. The left eye was, however, amblyopic. Vision in the right eye was −0.75 D sphere with +2.50 D cylinder, axis 80°=6/9, and in the left −2.25 D sphere with +2.50 D cylinder, axis 95°=6/24.

Teeth.—A dental surgeon reported as follows :

Congenital deformity of the face: many temporary teeth missing.

Present teeth are these: $\frac{6 \quad 321 \quad 13 \quad 6}{6^* \quad 21 \quad 12 \quad 6^*}$.

Upper incisors very prominent with narrow maxillary arch. *X* rays of teeth show retained roots with apical abscess $\underline{|7}$. Retained root $\overline{77}$. Teeth marked* are septic roots.

Body.—The second and third digits of both feet were found to be webbed. No other skeletal deformities were found.

Treatment.—A series of operations was carried out. A dacryocystorhinostomy was performed on the right side and a week later the lymphangioma of the upper lip was subjected to surgical diathermy. A dacryocystorhinostomy was performed on the left side. Eleven months later a further wedge of tissue was excised from the inner portion of the upper lip, and later still a plastic operation was performed on the right ear by transposition of skin flaps, free mobilization and advancement of the auricle to a higher point of attachment to the skull. The preauricular fistula on the right side was found to be very extensive, the deep portion of it containing a little thick pus. This area was explored down to a narrow opening into the bone above the ear, which was curetted. Later a similar plastic procedure was carried out upon the left ear, with exploration of the corresponding fistula, which did not, however, reach the bone. Substantial improvement in the patient's condition and appearance resulted.

FIG. 1.—Condition before treatment, August 4, 1950, full face.

Summary

A case of mandibulo-facial dysostosis is described with records of similar cases collected from the literature.

The condition is due to delayed or defective development of the mesoderm of the maxillary process about the end of the second month of foetal life.

Multiple congenital defects are described in association with this syndrome.

The variable nature and extent of the defects renders routine treatment difficult. Each case has to be treated on its individual merits.

Fig. 2.—Condition before treatment, August 4, 1950, left lateral view.

FIG. 3.—Condition before treatment, August 4, 1950, right lateral view.

I wish to record my sincere thanks to Mr. M. E. Spencer-Harrison for his co-operation in performing the ear, nose and throat operations mentioned above and for his assistance in the preparation of this paper.

My thanks are also due to Mr. Stacey for the preparation of the clinical photographs and to Miss Bryden and Miss Gower for secretarial help.

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SCLERAL RESECTION—LAMELLAR OR PENETRATING?*†

BY

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It affords me much pleasure to dedicate this short paper to Professor Dr. Karl Lindner as he has always been much interested in the subject of detachment of the retina in all its aspects. It was he who re-introduced Müller's operation for the treatment of cases of retinal detachment with unfavourable prognosis (Lindner, 1933) and his operation was taken up by Pischel (1945), Borley (1949), and Vail (1948) in the United States, and later by Lister (1951a) Philps (1951) and myself (Shapland, 1951a) in Great Britain. In the summer of 1949, I, in my turn, modified Lindner's operation in three ways :

(1) by making the excision of the scleral strip " lamellar ", i.e. leaving in situ a very thin film of the deepest scleral lamellae to protect the choroid,

(2) by combining the lamellar sclerectomy with, most usually, chemical (caustic potash), but occasionally with diathermy coagulation over the retinal tears,

(3) by the use of silk sutures for approximating the two edges of the excised scleral strip.

Lamellar scleral resection has also been performed since September, 1950, in the department of ophthalmology of l'Hôpital de l'Antiquaille by Dr. Paufique and his assistants, and for the purpose of this paper I thought it would be of interest to compare published results of full-thickness sclerectomies with those obtained by the lamellar operation by Paufique and myself.

In the title I have used the term " penetrating " to denote the full-thickness scleral resection ; the results obtained by the pioneers of this operation—Müller himself, Blaskovics, Leitner, Elschnig, Török and Koch were reviewed by Borley (1949), who collected a total of 82 operations performed on all types of detachments with myopia the preponderant underlying condition, and stated that cures were claimed for eighteen cases (approximately 22 per cent.) and improvements in 30 per cent. Leopold (1945), also reporting on these and other pioneers of Müller's operation, collected 121 cases from the literature, 25 (21 per cent.) successfully re-attached and 31 (26 per cent.) with partial or temporary re-attachment. It is indeed surprising that with such apparently satisfactory results for an otherwise almost hopeless condition Müller's operation was not more extensively performed in the pre-Gonin

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† Dedicated to Professor Lindner on the occasion of his 70th birthday.

days, yet it seems to have been almost abandoned with the advent of Gonin's work on the fundamental importance of retinal holes in the aetiology of simple detachment of the retina and the successes obtained first by his operation of cautery puncture, and later by the various forms of diathermy operation all of which were directed towards the seclusion of these retinal defects. As we have seen, however, the full-thickness scleral resection operation was revived by Lindner (1933) with modifications for cases of retinal detachment with unfavourable prognosis, and his published results together with those of Pischel, Borley, and Vail in the United States, and Lister, Philps, and myself in the United Kingdom as shown in Table I.

TABLE I

PENETRATING SCLERAL RESECTIONS

Author and Date	Number	Results			
		Cured		Improved	
		No.	Percent.	No.	Percent.
Pioneers (quoted by Leopold, 1945)	121 cases	25	21	31	26
Pioneers (quoted by Borley, 1949)	82 operations	18	22	—	30
Lindner (1933)	12 eyes	3		7	
Lindner (1949)	36 eyes	6	17	10	28
Pischel (1945)	15 operations	2		4	
*Vail (1948)	8 cases	3½		—	
Borley (1949)	28 operations	9		8	
Lister (1951a)	34 cases	11	33	3	9
Philps (1951)	19 cases	11½		—	
Shapland (1951b)	6 cases	0		2	
Totals	158	46	29	34	22

* Resections performed for cases of retinal detachment associated with scleral staphyloma. (Percentages recorded only if numbers exceed 30.)

The pioneers, therefore, could claim some 21 to 22 per cent. of cures using in the main Müller's technique whilst with the later operators employing Lindner's method the successes have risen to about 29 per cent. On the other hand Lister (1951b), at the Oxford Congress 1951 gave a summary of the results of scleral resections performed for retinal detachment at the City Road branch of Moorfields from July, 1947, to May, 1951, and of 102 penetrating resections only 22.5 per cent. were cured. It seems, therefore, that only about one quarter of detachments operated upon by the full-thickness method are likely to become replaced.

To turn now to my operation of lamellar sclerectomy ; an analysis of my first fifty cases taken in chronological order since July, 1949, and omitting all full-thickness operations, is shown in Table II (opposite).

Barut (1952) has reported on the results from the Service d'Ophtalmologie

TABLE II

LAMELLAR SCLERAL RESECTIONS

			Total	Cured		Improved	
				No.	Per cent.	No.	Per cent.
Cases Operated			50	19	38	14	28
Previous Diathermy			30	11	37	8	27
No Previous Diathermy			20	8	40	6	30
AETIOLOGY	Aphakia :	Congenital Cataract Discission	5	1		—	
		Extracapsular Extraction	3	1		—	
		Intracapsular Extraction	1	1		—	
		Others	2	—		1	
		Total	11	3	27	1	9
	Myopia :	High (over 10D)	11	2		3	
		Moderate (5–10D)	6	6		—	
		Low (under 5D)	10	4		4	
		Total	27	12	44	7	26
	Emmetropia and Hypermetropia (senile 4; cystic 5 ; traumatic dialysis 1; inflammatory 1; doubtful 1)		12	4	33	6	50

de l'Hôpital de l'Antiquaille, where lamellar scleral resection combined with diathermy coagulation has been employed since September, 1950. In 116 eyes operated upon, he claims successful repositions dating for at least 3 months in sixty (51.8 per cent.), part success in nine (7.7 per cent.), and failures in forty-seven (40.5 per cent.). My figures for fifty eyes are 38 per cent. cured, 28 per cent. improved, and 34 per cent. failures. It would seem, therefore, that in about 60 per cent. of cases in which the lamellar scleral resection has been employed a success or a substantial improvement has been obtained. It is true that my figure for improvements is considerably higher than that of Paufique but I have had to include patients up to August of this year to obtain my first fifty lamellar operations, and it may well be that when this year's patients are reviewed again early next year (as is my custom) some of those now classed as " improved " will have to be relegated to the column of " failures ". It is a curious fact, however, that with this operation the retina is often quite slow in becoming replaced, in one of the senile detachments the retina took a whole year to go back and in one of the low myopes a good 5 months, so I hope also that a few of the "improved" may be transferred to the column of " cures ".

There is, I think, general agreement that the operation of lamellar scleral resection is considerably safer than the full-thickness procedure, also easier to perform and probably somewhat less time-consuming. As the results shown in this paper are so much superior to those of the full-thickness procedure, despite the fact that I have been operating on the most unpromising and desperate cases sent to my clinic at Moorfields from all over Great Britain, it would appear that lamellar sclerectomy should now supplant the full-thickness procedure and should be employed in the following types of case:

(1) As a primary procedure in senile detachments, these often show multiple peripheral tears in an atrophic retina and are a very definite indication.

(2) As a primary procedure in detachments occurring in myopia, especially those with multiple and widely-spaced rents in front of the equator of the globe; these have done very well in my series especially those in the more moderate grades.

(3) As a primary procedure in old-standing detachments, especially inferior detachments with multiple " striae retinae ".

(4) As a primary procedure in detachments occurring in aphakia especially in those in which no hole can be found. In this respect it must be noted that Schepens (1951) has stated that degenerative changes near the ora serrata are more than twice as frequent in aphakic as in phakic subjects and he found that the average number of " breaks " for 79 eyes was 4.45 per eye in this situation. My operation is, therefore, especially indicated here as a mild, but widespread, choroidal reaction is engendered directly behind the ora serrata.

(5) As a primary procedure in cases showing retraction of the vitreous such as occurs after vitreous haemorrhage, however produced, in old-standing detachments and again in aphakia. It should be noted, however, that with massive vitreous retraction and a total detachment of the retina no surgical procedure so far devised is likely to be of any avail.

(6) Detachments which have been operated upon unsuccessfully by diathermy; these usually exhibit secondary tears but occasionally a mal-reposition with retinal tension folds results and in both these groups of cases a sclerectomy rather than a further diathermy is indicated.

(7) Traumatic detachments, especially those consequent upon intra-ocular foreign bodies (which in general have a very poor prognosis), and also those associated with large peripheral dialyses.

(8) In general retinal detachments which do not respond well to rest and double padding. For Paufique this is a most important indication, and his adage is, " *la rétine n'a pas obéi au repos, elle n'obéira pas à l'intervention* ", but according to Barut (1952), with whom I surely agree, " *elle obéira peut-être à l'intervention, à condition que celle-ci comprenne une résection sclérale* ".

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JOHN DALTON, F.R.S., D.C.L., LL.D., CAPTAIN JOSEPH HUDDART, F.R.S., AND THE HARRIS FAMILY*

HISTORICAL NOTES ON CONGENITAL COLOUR BLINDNESS

BY

J. W. CRERAR AND J. A. ROSS

Maryport *Bridge of Allan*

THESE three names, all of Cumbrians, are closely associated in the early history of congenital colour blindness. John Dalton (1798) made careful and detailed observations on his own and other cases which are universally recognized, but he was not, as is commonly and erroneously believed, the first to draw attention to this condition. The early use of the term "Daltonism" no doubt fostered such a belief, so that the name of Joseph Huddart (1777) is almost forgotten, although it was he who first drew attention to "supernatural vision", as it was then called, and was the first to use coloured objects to test those affected and to record their reactions. He also noted the occurrence of colour blindness in male members of the same family who were Quakers "among whom a general uniformity of colours is known to prevail". Our quest originated in a reference, in a brief biography of Joseph Huddart, to a letter† giving "An Account of Persons who could not distinguish Colours", written by him to the Rev. Joseph Priestley, F.R.S. Priestley read this letter to the Royal Society on February 13, 1777, at which time Dalton was only in his 11th year.

Joseph Huddart (1741–1816), born in Allonby, a village near Maryport in Cumberland, had a remarkable career. The only son of a fisherman, he followed his father's occupation until 1768 when he had a brig built at Maryport in which he traded with Ireland and North America. He entered the service of the Honourable East India Company in 1773 as fourth officer and on a voyage in that year surveyed the west coast of Sumatra. He returned home in 1775, and in 1777 surveyed the St. George's channel. In 1778 he rejoined the company as chief officer, and later captain, of the *Royal Admiral*.

Retiring from the sea in 1788, he devoted himself to hydrographic and survey work on the west coast of Scotland and numerous harbours and docks. He was elected an Elder Brother of Trinity House and F.R.S. in 1791. Throughout his life he had been greatly interested in optical problems as evidenced by the letter to Priestley mentioned above, and by a paper he read to the Royal Society on "Horizontal Refraction" in 1796.

He died in London in 1816. A monument to his memory was erected by his son, Sir William Huddart, in Christ Church, Allonby, to whose first

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† Now preserved in the British Museum.

vicar, the Rev. Thomas Wilson, the young Joseph Huddart had been indebted for his education.

Huddart's was the first reliable record of inability to distinguish colours. In the case recorded by Turberville of Salisbury (1684), a young girl is said to have been unable to distinguish colours except black and white, but as she is also said to have been able to read in the greatest darkness and to have seen terrifying bulls and bears invisible to others, it seems evident that she suffered in fact from some cerebral or mental disorder. No objective evidence is given, only the statements of the girl herself.

In his letter to Priestley, Huddart tells of his 10 years' acquaintance with Harris [Thomas] " by trade a shoemaker at Maryport ", and of his frequent conversations with him,

> an intelligent man and very desirous of understanding the nature of light and colour, for which he had attended a course of lectures on natural philosophy . . . I believe he could do no more than guess the name of any colour; yet he could distinguish white from black. Dark colours in general he often mistook for black.
>
> He had two brothers [actually three] in the same circumstances as to sight; and two other brothers and sisters who, as well as their parents, had nothing of this defect.

One of these brothers [Jonathan], a master mariner, Huddart met in Dublin in December, 1776, and tested carefully with striped ribbons, " not having a prism by me ": of four black stripes of exactly the same shade he declared three to be brown and only one black, the light green he called yellow, a reddish tinge he called a sort of blue.

> But he was most of all deceived by the orange colour; of this he spoke very confidently, saying, " This is the colour of grass; this is green ".

This is the first recorded use of coloured objects for testing colour vision ; a method followed and extended by John Dalton in his own case about 13 years later (1790).

Huddart's communication attracted little attention, only the two following references being made to it during the 17 years that elapsed before Dalton's communication:

> (*i*) In 1778 the Rev. Michael Lort wrote to the Royal Society describing the case of Mr. J. Scott. This letter contains the first reference to colour-blindness in a female—a member of the Scott family (Lort, 1778).
>
> (*ii*) In 1779 the Abbé Rozier translated Huddart's paper into French and recorded the case of Collardeau, a painter (Rozier, 1779.)

John Dalton (1760–1844), in his historic paper " Extraordinary Facts relating to the Vision of Colours, with Observations ", read on October 31, 1784, before the Literary and Philosophical Society of Manchester, mentioned that he had read and re-read the account of the case of Mr. Harris of Maryport in Cumberland in the *Philosophical Transactions* (Huddart, 1777) and mentioned Rozier's translation. Having an acquaintance in Maryport

(Joseph Dickinson) he had asked him to propose some queries to the surviving colour-blind Harris brother [actually two brothers, Joseph and John]. This important paper is so well known that it is unnecessary to refer to it in detail. In his correspondence (1793–1794) with Dalton, Joseph Dickinson identified by name the four colour-blind members of the Harris family: II, 1 and 8, Thomas and Jonathan (the Master Mariner), both long since dead, and II, 2 and 7, Joseph and John, the two living brothers.

Incidentally it may be mentioned that Dickinson himself had married Mary, the only daughter of Thomas Harris, and that his only son Isaac was colour-blind.

Two curious pieces of information may be of interest. Dalton had surmised that the cause of his odd vision might be " some colouration of the humours of his eyes, probably some modification of blue in the vitreous ", and he desired that his eyes should be examined after his death. Dr. John Ransome removed them and found that " the aqueous humour, the vitreous and its hyaloid membrane were perfectly colourless ". One of these dissected eyes is still to be seen at Dalton Hall, Manchester.

Under the great council table in Manchester Town Hall, where it had been used as a footstool, a bust of John Dalton was discovered by a friend and by him cleaned and restored. It was sent to the Chemistry Department at Cambridge, and on arrival consigned to a storeroom. Many years later this bust was recognized by Professor A. R. Todd and given its present place of honour in his Senior Research Laboratory in Pembroke Street, Cambridge.

The Harris Genealogical Table

Dr. Julia Bell gives a Table compiled from Dalton's statements and the Records of the Society of Friends, and expresses doubt as to II, 7, surmising that he was colour-blind (Bell, 1926). Her table and ours are set out in the Figure.

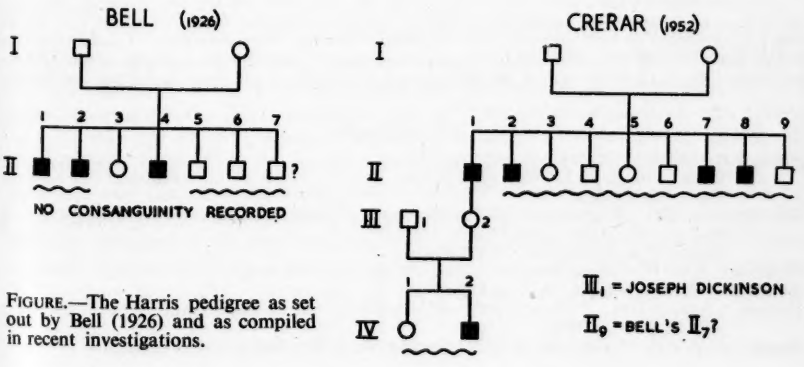

FIGURE.—The Harris pedigree as set out by Bell (1926) and as compiled in recent investigations.

One of us (J.W.C.), who for many years practised in Maryport, had the opportune good fortune to have access to the Netherhall (Maryport) Estate Records ; to have certified copies made of entries in the Friends' Registers at Wigton, Cumberland ; and especially, thanks to a member of the family, to peruse the carefully detailed Harris papers which give the irrefragable pedigree of the family of William and Hannah Harris, and incidentally of the maternal descent of the immortal Joseph, Lord Lister.

Anthony Harris (1755–1795) the youngest of the family (II, 9) was a master mariner and was drowned at sea ; he married Isabella Bull of Dublin, and they had eight children. The fifth, Elizabeth, was the grandmother of the late Mrs. George Cadbury, D.B.E. The sixth, Isabella, born in Maryport in 1792, married Joseph Jackson Lister in 1818, and the fifth of their eight children was Joseph, Lord Lister (1827–1912). She was the grandmother of Sir Rickman Godlee, P.R.C.S.—the biographer of his uncle Joseph—and of Sir William Lister, K.C.V.O., the oculist. She is beautifully portrayed in Godlee's biography.

Anthony Harris had normal vision. Had he been colour-blind and had Isabella transmitted the defect to her male descendants, would Lord Lister, Sir Rickman Godlee, and Sir William Lister have become surgeons ? It seems impossible that an ophthalmologist could be colour-blind, but some 30 years ago a general surgeon of the highest standing among his fellows was found by one of us (J.A.R.) to be as colour-blind as was John Dalton.

Summary

The particular contributions of John Dalton, Joseph Huddart, and the Harris family to the subject of congenital colour blindness are examined. While the outstanding importance of Dalton's work is not overlooked or minimized, Huddart's claim to priority is confirmed and fortified.

The descent of Lord Lister, Sir Rickman Godlee, and Sir William Lister from Isabella Harris is indicated.

Acknowledgments are due first and foremost to Dr. Julia Bell and her encyclopaedic work—a storehouse of accurate and detailed information; to the member of the Harris family who placed the Harris papers at our disposal; to Mr. Robert Ritson, barrister-at-law, London, for the transcripts of Huddart's and of Dalton's communications; and to the Librarians of the B.M.A., of Tullie House, Carlisle, and of the Manchester City Library for their invaluable assistance.

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INTRA-OCULAR OPERATIONS IN EGYPT*

BY

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THE handling of intra-ocular operations in Egypt differs from that in Europe and the Western countries because of the frequent infection of patients with trachoma, which leads to the following complications:

(*i*) scarring of the lids (trichiasis and entropion), conjunctiva, limbus, and cornea (trachomatous keratitis);

(*ii*) affections of the limbus;

(*iii*) corneal scarring by nebulae and leucoma.

The last-named may also be due to purulent ophthalmia, which is more prevalent in Eastern countries (Egypt, Palestine, Syria, India, etc.). In Egypt many patients are also affected by cataract, glaucoma with sunken globes, narrow palpebral fissures, and narrow or obliterated fornices. The sphincter iridis in brown and black eyes is stronger than that in green or blue eyes, and the extra-ocular muscles are also stronger, so that "squeezers" during operations are more often found in the East, and the pupil sometimes does not attain full or even half dilatation, even under strong mydriatics.

Trachoma, which affects about 95 per cent. of the population in Egypt, is mainly responsible for these complications, but gonococcal infection, and Koch-Weeks, Morax-Axenfeld, pneumococcal, and other bacterial infections cause many complications in secondary cataract. In the summer the majority of hospital out-patients (46 per cent.) attend on account of gonococcal infection, and 23 per cent. on account of Koch-Weeks and Morax-Axenfeld infection. These provoke such complications as perforated ulcers, nebulae, and glaucoma with secondary cataract.

In 1950, I visited a number of hospitals in Paris, and there happened to see a smear taken from a small child who was being treated for conjunctivitis. When I asked the laboratory assistant about the percentage of cases affected with gonococcal and Koch-Weeks ophthalmia or other micro-organisms, she replied that she did not expect to see a single case infected with gonorrhea during the whole year. The child in question was suffering from a mild pneumococcal infection, and the assistant added that these were also very few.

In Egypt, gonococcal infection is prevalent throughout the whole year and becomes epidemic from June to November (MacCallan, 1916). In 1922 certain cases of diphtheritic conjunctivitis (Girgis, 1923) were complicated with gangrene of the orbit leading to the death of the patient, or to nebulae and leucoma

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of the cornea. The affection of the cornea by pannus in trachoma is manifested by the extension on to the cornea of blood vessels, and the affection of the limbus is seen in scarring of the pits known as Herbert pits. The blood vessels derive from the conjunctival vessels and introduce themselves between the corneal epithelium and Bowman's membrane; these pannus vessels must be distinguished from those due to the healing of corneal ulcers or to interstitial keratitis. In some cases of trachoma, Bowman's membrane becomes destroyed here and there, and the cellular infiltration gains access to the stroma of the cornea, where it gives rise to permanent changes in its transparency and curvature. Other results of pannus are weakening of the corneal stroma and bulging. Pannus leads to a form of degeneration of the conjunctiva in which the epithelium becomes thickened by the swelling and proliferation of the cells. This condition is most likely caused by colloid degeneration, which makes the conjunctiva friable, so that the operations of fixing the globe and making a good conjunctival flap, and corneal and corneo-scleral section, become more difficult. In badly affected cases of trachoma of the bulbar conjunctiva, the fornix may be contracted and shrunk.

Anaesthesia

These complications make it necessary to have the glaucoma and cataract cases well hypotonized and completely quiet so that they do not squeeze and interfere with the operation. Prof. Barraquer of Barcelona uses curare in intra-ocular operations to keep the eye quiet and relaxed, or, to use his expression, "with the vitreous asleep". The nature and use of curare have recently been described by Agarwal and Mathur (1952), but as this drug is rather dangerous I have been searching for something to take its place. During a systematic investigation* of the pharmacological properties of α-substituted glycerol ethers, it was found that some of these compounds produced muscular relaxation and paralysis. Administration of small quantities subcutaneously to laboratory animals caused tranquilization, muscular relaxation, and a sleep-like condition from which they could afterwards be aroused. Of the compounds examined, α: β.dihydroxy-γ-(2-methylphenoxy)-propane, subsequently named "Myanesin", was found to be the most potent and also to possess the widest margin between the lethal and therapeutic doses.

I therefore tried "Myanesin" in my private and hospital practice. I have had good results in glaucoma and cataract, and even in simple iridectomy after adherent leucoma, with or without tension, a condition which in Egypt rather frequently follows purulent ophthalmia, and is mostly of gonococcal origin. I have used "Myanesin" in about seventy such cases of adherent leucoma without anaesthesia, and with no complications even in young patients, and I have also tried it in combination with akinesia in cataract and glaucoma.

One tablespoonful of the "Myanesin" elixir was administered 2 hours

*Carried out in the Research Laboratories of British Drug Houses Ltd.

before the operation; this was followed by another dose 30 min. before the operation. This dose was used whether the eye became tensed or not, and in fact, I found it was better to use it in cases with tension as the tension then became lowered; after 30 min. the eye muscles were relaxed and hypotony of the eye was seen, the vitreous was "asleep" and the operation could be carried out with safety. Recently I have given a larger dose of the elixer: one tablespoonful 2 hours before, another dose 1 hour before, and a third 30 min. before the operation.

In cases of glaucoma with high pressure, the tension is lowered before the operation and complications are lessened or abolished. Prof. Barraquer uses curare in all intra-ocular operations for the purpose of keeping the vitreous "asleep", but in my opinion "Myanesin" elixir may very well replace curare, since it is not so dangerous in use. A colleague who saw Prof. Barraquer using curare, and wanted to use it in Egypt but was afraid of possible complications, is now also using "Myanesin" in all his intra-ocular operations with complete satisfaction.

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Brit. J. Ophthal. (1953) **37**, 188.

CASE NOTES

INJURY SIMULATING CONGENITAL ANOMALY*

BY

L. STANTON-COOK

Sydney, Australia

IT is remarkable that in some inflammatory conditions (particularly chronic anterior uveitis) the end results may come to resemble closely certain congenital abnormalities. For example, the arrangement of new vessels in the inflammatory membrane covering the front of the lens in chronic iritis often mimics that seen in the normal pupillary membrane. The new vessels may show a sectorial arcaded arrangement and may even in some cases arise from the lesser circle.

The present case is published to demonstrate how the effects of injury to the optic nerve may come to resemble persistence of the hyaloid artery and its glial cone. Without the definite history of trauma this case would undoubtedly have been considered developmental.

Case History

The patient, a boy of 9½ years, was injured in 1929 by another boy up a tree thrusting a bamboo pole into his right eye. He was seen the same day by Mr. Temple Smith of Sydney who found a haemorrhage in the vitreous, and diagnosed a rupture of the optic nerve or a haemorrhage into its sheath. He later observed the haemorrhage organizing. No perception of light was present.

I saw the patient in 1936 when he was 15½. The right eye was blind. The left eye normal with visual acuity 6/5. There was no external evidence of injury. The right pupil was inactive to direct stimulation but reacted consensually, and (sluggishly) to accommodation and convergence. The pupil dilated under H. and C. but not quite as well as the left.

The examination of the right fundus shows a cone of " proliferation " with base formed by the whole of the disc stretching forward into the vitreous; it looks like an aerodrome wind-sock but glistens white like a stalactite. At the apex of the cone, fine straight fibrils extend into the vitreous and are lost. Pigment partially surrounds the base of the cone.

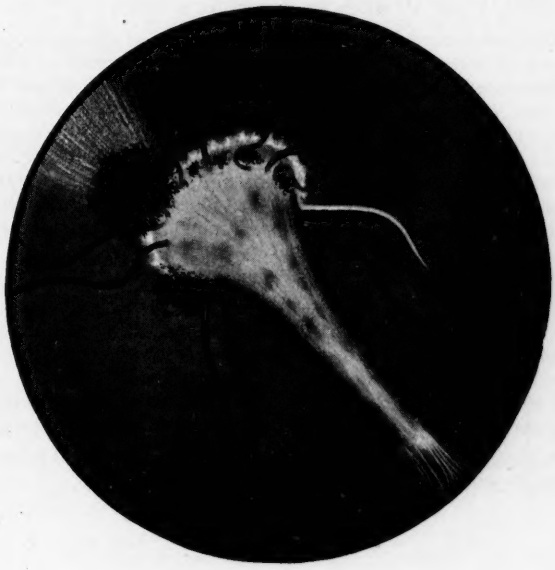
The general appearance is as depicted in the Figure† but it is impossible to convey the glistening whiteness with a superimposed greenish sheen, and the somewhat crenated surface, all of which combined to give the stalactite effect. The pencilling in the right upper quadrant is intended to indicate what appeared to be a slight, flat, local, retinal separation.

* Received for publication November 6, 1952.

† The Figure was prepared by Theodore Hamblin Ltd. under direction from an amateur painting made at my rooms.

It is obvious that without the history of injury and the immediate examination by Mr. Temple Smith the most likely diagnosis would have been persistence of the hyaloid artery and proliferation of its glial cone.

This case illustrates the fact that serious injury to the eye can occur without external evidence of trauma. The importance of obtaining a detailed history, even involving obstetric details, in any case suggestive of congenital anomaly but possibly attributable to trauma cannot be overlooked. It is possible that cases of retinal septum, macular coloboma, "congenital" detached retina, and glial proliferations on or near the disc may in some cases be post-natal in origin, though most are undoubtedly developmental.



FIGURE

Summary

A case is described of traumatic rupture of the optic nerve presenting the appearance of congenital persistent hyaloid artery and glial cone.

My thanks are due to Mr. Temple Smith, who examined the boy on the day of his injury, for his notes; and to Professor Ida Mann for the benefit of her vast experience and suggestions.

CORRESPONDENCE

REQUEST FOR REPRINTS OF ARTICLES ON STRESS AND THE *ADAPTIVE HORMONES*

To the Editorial Committee of the BRITISH JOURNAL OF *OPHTHALMOLOGY*

DEAR SIRS—In perusing the current literature with which your Journal is concerned, we note that an ever-increasing number of articles deal with problems pertaining to research on "*stress*" and the so-called "adaptive hormones" (ACTH, STH, corticoids, adrenergic substances, etc.).

We are writing you because, in our opinion, the success of research in this complex and rapidly developing field largely depends upon the prompt availability and evaluation of relevant publications, a task for which we should like to solicit your readers' assistance.

In 1950, our Institute initiated the publication of a series of reference volumes entitled "*Annual Reports on Stress*" (Acta Medical Publishers, Montreal) in which the entire current world literature is surveyed every year (usually between 2,000 and 4,000 publications). Up to now, we have had to compile the pertinent literature partly from medical periodicals, monographs, and abstract journals, and partly from reprints sent to us by the authors themselves. Of all these, reprints have proved to be the best source of data which we felt deserved prompt attention in our annual reports. Hence, in the past, we have sent out several thousand individual reprint requests to authors whom we knew to be currently engaged in research on stress and allied topics. Even this procedure did not give us the wide coverage which would be desirable, because it is materially impossible to contact all these authors individually and it often takes too much time to get the requested reprints.

It is evident that in order to insure prompt inclusion of publications in the annual reports, these surveys must develop into a cooperative effort between the authors of original papers and the reviewers. This cooperation has been greatly enhanced of late by the publication of announcements, in several medical journals, encouraging investigators interested in stress research to send us their reprints as soon as they become available.

We should be grateful if by the publication of this note, you would bring this problem to the attention of your readers.

We are, Gentlemen,

Very sincerely yours,

HANS SELYE,
ALEXANDER HORAVA.

INSTITUTE OF EXPERIMENTAL MEDICINE AND SURGERY,
UNIVERSITY OF MONTREAL, CANADA.

January 21, 1953.

BOOK REVIEW

Retrolental Fibroplasia and Other Forms of Pseudo-Glioma. By C. H. O. M. VON WINNING. 1952. Pp. 116, 32 tables, 63 figs., 314 refs. The Hague.

This is an excellent review of the literature on retrolental fibroplasia together with a report of the first 37 cases of this condition which have occurred in the Netherlands

between 1948 and 1952. Incidence, clinical aspects, pathology, aetiology, prophylaxis, and treatment are each considered in turn. An interesting contribution is the use of slit-lamp microscopy by means of which an increased aqueous protein content without increase in cells in the anterior chamber may be observed in the active phase of retrolental fibroplasia. New-vessel formation on the iris is also mentioned, and the notion of anoxia as a causative agent is favoured.

The second section comprises a valuable account of the differential diagnosis of retinoblastoma and retrolental fibroplasia: it is unfortunate that the unhappy term "pseudoglioma" is used in the title of this section of the book (and also frequently in the text) in view of the high standard of thought and observation, clinical and pathological, with which these several conditions are described. The following conditions are described and illustrative case reports appended in each instance: hypertrophy of primary vitreous, ablatio falciformis retinae, retinal dysplasia, metastatic ophthalmia, tuberculosis, toxoplasmosis, exudative retinitis of Coats.

The essential points of differential diagnosis are given in the short third section.

In general, this book is a valuable contribution to an important subject, and it is a pity that the nine plates are not of uniform quality.

NOTES

Ophthalmological Society of the United Kingdom

The society holds a considerable stock of certain volumes of the *Transactions* since their first publication in 1881. The Council would be glad to present to members such available volumes as they may desire. No charge will be made beyond the cost of packing and postage. The volumes available are:

Volume	*Date*	*Volume*	*Date*	*Volume*	*Date*
1	1881	7	1887	35	1915
2	1882	8	1888	45 pt. 1	1925
3	1883	9	1889	45 pt. 2	1925
4	1884	11	1891	61	1941
5	1885	12	1892	67	1947
6	1886	33	1913	68	1948

Applications, which will be dealt with in rotation, should be sent to the Honorary Secretary, Ophthalmological Society of the United Kingdom, 45 Lincoln's Inn Fields, London, W.C.2, before July 31, 1953.

South Western Ophthalmological Society—Southern Ophthalmological Society

The joint meeting at the Bristol Eye Hospital, Bristol, which was planned for May 9, has been postponed to Saturday, May 30, at 2.15 p.m.

Anthony Palin, Nigel Cridland } *Hon. Secretaries.*

Royal Eye Hospital Clinical Society

The March meeting will be held at the Hospital on Wednesday, March 25, 1953, at 8 p.m. Mr. Murray A. Falconer will speak on "Visual Field Changes in Compressions of the Optic Nerve, Chiasm, and Tract".

Corrigendum

British Journal of Ophthalmology (1953), **37**, 125, line 6: for "glaucomatous" read "trachomatous".

OBITUARY

JAMES COLE MARSHALL

WE announce with regret the death of Mr. J. Cole Marshall, M.D., F.R.C.S., which occurred suddenly on Christmas Eve at his home in Rickmansworth, Herts.

James Cole Marshall, born in 1876 at Blandford, Dorset, studied at Bart's and qualified in 1900. His first interest was gynaecology, and his M.D. degree, which he took in 1904, a year after taking the Fellowship, was in this subject. Soon afterwards, however, he was attracted to ophthalmology, and decided to make that his specialty.

Although Cole Marshall's main work was done at the Western Ophthalmic Hospital, where he was a member of the honorary staff from 1913 to 1946 and senior surgeon for 11 years, he held other appointments at the Royal Waterloo Hospital, the Lambeth L.C.C. Hospital, and the Northwood and Pinner Hospital. He was further associated with several institutions for the blind, such as the Sunshine Home and the Royal London Society for Teaching and Training the Blind. He was also Oculist to the Royal Academy of Music, and during the first world war he served in the R.A.M.C. as ophthalmic specialist to the Army of the Rhine.

Cole Marshall was an efficient all-round surgeon, skilful, careful, and deliberate as an operator; sound in clinical judgement; and thorough in examination. He was one of the very first in Great Britain to practise the modern operative treatment of retinal detachment, which he continued to study with increasing enthusiasm and practised with remarkable success for the rest of his medical career. This success was primarily due to his careful and prolonged survey of the fundus for retinal tears, etc. These were all systematically plotted on his well-known muscle charts, which are still widely used. His capacity for work and his energy in this and other respects were outstanding, and his methods and example in training a long succession of house-surgeons and registrars were an inspiration to his colleagues. It is no exaggeration to say that he founded a school of detachment surgery at the Western. Although he tried out most of the various techniques, he ultimately remained faithful to puncture diathermy, which he preferred to surface coagulation. In this he was supported by the work of the Weekers in Belgium, who have shown that the puncture technique facilitates the downgrowth of subconjunctival cells, resulting in a firmer scar. He had a craftsman's pride in the quality of his scars, not too weak and not too dense—the latter, owing to scar tissue contraction, predisposing to secondary tears.

In 1935, he gave the Middlemore Lecture at the Birmingham Eye Hospital; in 1938 he was appointed Hunterian professor at the Royal College of Surgeons, and his book "*The Operative Technique of Retinal Detachment*" was published in the following year.

Cole Marshall was a modest, delightful, and charming personality with a keen sense of humour, interested in music and in painting, and no mean judge of quality in both. He was a well-balanced and lovable person, affectionately admired by patients and colleagues.

In 1905 he married Miss Margaret Compton, who, with their three daughters, survives him. He was singularly fortunate in a happy home life. Between the wars he moved from Albion Street to Rickmansworth, where he built a most attractive house and developed a beautiful and well-timbered garden. The latter was a perennial source of pleasure in that he could there enjoy the twin delights of two favourite hobbies, gardening and bird-watching, but he never lost interest in the affairs of the Western Ophthalmic Hospital, where his death has been felt by all as the personal loss of a friend.